ORIGINAL

STATE OF CALIFORNIA

SCIENTIFIC REVIEW PANEL

ON AIR CONTAMINANTS

AIR RESOURCES BOARD, and DEPARTMENT OF HEALTH SERVICES IDENTIFICATION REPORT	Perchloroethylene as a Toxic Air Contaminant

REPORTER'S TRANSCRIPT

June 10, 1991

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A C T I O N

	Motion	Vote
Board Member Glantz, to adopt staff report.....	119	145

Scientific Review Panel

June 10, 1991

University of California

Irvine, California

- - P R O C E E D I N G S - -

CHAIRMAN PITTS: Good morning, ladies and gentlemen. Welcome again to another meeting of the SRP.

Our first item is consideration of Air Resources Board, Department of DHS, report regarding identification of perchloroethylene as a toxic air contaminant.

Now, I gather that the staff of the ARB will present the Part A. And, members here for Part A are -- well, Genevieve is not here, she is still in Greece, right? probably on some island out there wondering what's this air pollution stuff. But, Joan and Barbara, you are going to be representing this?

All right. That is Dr. Joan Denton, and Ms. Barbara Cook, and if you would come up and make the presentation.

BARBARA COOK: Thank you, Dr. Pitts, and good morning to all of the members of the panel.

Today we will discuss the scientific evidence in Parts A and B of the perchloroethylene document. We believe that this evidence supports the identification of

this compound as a toxic air contaminant.

This transparency -- to your rear -- shows the chemical structure of perchloroethylene, a chlorinated hydrocarbon with a double bond between its two carbon atoms.

The Air Resources Board and the Department of Health Services selected perchloroethylene for your consideration for following reasons:

The international agency for research on cancer listed perchloroethylene as a possible human carcinogen in 1987. In 1986, the Environmental Protection Agency's health risk assessment staff proposed that perchloroethylene be classified as a probable carcinogen; however, at that time, the agency's scientific advisory board believed that perchloroethylene should be classified on a continuum between Group B2, probable carcinogen, and Group C, possible carcinogen. Until this controversy is resolved, the agency's official position is that it is a Group C.

As of April 1, 1988, perchloroethylene was listed by the State of California as a chemical known to cause cancer under the Proposition 65 program. In addition, the federal government listed perchloroethylene as a hazardous air pollutant in the amendments to the 1990 Clean Air Act.

Perchloroethylene is widely used in California, and it has been demonstrated in indoor and outdoor air in this state.

In my presentation I will summarize the following Part A exposure information in the order listed:

Production and usage in California;

California emissions;

Exposure levels in California;

Persistence.

Production and usage. California has one perchloroethylene production facility, with a capacity to produce 25,000 tons of the solvent per year. Based on the 1987 survey of California halogenated solvent distributors, approximately 19,000 tons of perchloroethylene are used each year in the state.

The greatest use of perchloroethylene is in dry cleaning and degreasing. Other examples of products and processes in which perchloroethylene is used are paints and coatings, adhesives, aerosols, specialty chemicals, printing inks, silicones, rug shampoos, and laboratory solvents.

Next, we will discuss emissions. Approximately 18,000 tons of perchloroethylene are emitted from production, distribution, usage, reclamation and disposal

of the solvent. Based in available information, we estimated that approximately 80 percent of 1987 perchloroethylene emissions were from dry cleaning and degreasing operations. We expect that current perchloroethylene emissions from dry cleaning are lower than those in 1987 for the following reasons:

Because perchloroethylene is a volatile organic compound and therefore an ozone precursor, it has been targeted for varying degrees of control by local air pollution control districts and several districts have mandated the use of control equipment for large dry cleaning operations.

The trend is toward using a single piece of equipment for both washing and drying clothes. This avoids the perchloroethylene emissions resulting from the manual transfer of clothes from washer to dryer.

Another reason is that there is an increasing number of large industrial cleaners using detergent and water instead of perchloroethylene.

And, finally, the adoption of hazardous waste regulations mandating the storage of filter and distillate residues in air-tight containers has also served to reduce the emissions.

If perchloroethylene is identified as a toxic air contaminant, the developments I have just mentioned

will be considered in the revised emission estimates for the control phase.

Next, exposure in California. Outdoor, or ambient exposure, will be discussed first, followed by near source and indoor exposure.

Based on data collected by the Air Resources Board's ambient toxic air contaminant monitoring network, the mean annual ambient population-weighted exposure for 20 million people living in urban California areas is estimated at 0.37 ppbv.

The Department of Health Services staff's best value of cancer unit risk is 54 X 10 -6 per ppbv; or, 54 cancers per million people continuously exposed to 1 ppbv of perchloroethylene over a 70-year lifetime.

Using this estimate, and assuming a statewide mean annual ambient perchloroethylene concentration of 0.37, up to 600 potential excess cancers are predicted among California's population of 30 million over a period of 70 years.

The Air Resources Board staff modeled eight perchloroethylene-emitting facilities in the south coast, in order to estimate emissions near sources. Seven of the facilities were degreasing operations, and one facility was an industrial clothes cleaner. Five facilities were located in or near the City of Industry,

and three were located in or near Burbank.

In the exposure estimates, only the contributions the modeled facilities made to perchloroethylene exposure are considered. An estimated 2000 maximally exposed individuals near the City of Industry are exposed to an ambient concentration of 6 ppbv, which is approximately 15 times the estimated statewide ambient average. And, I will remind you that the 6 ppbv is above any background perchloroethylene.

An estimated 600 maximally exposed individuals near Burbank are exposed to an ambient concentration of 3 ppbv, which is approximately eight times the estimated statewide ambient average.

If perchloroethylene is identified as a toxic air contaminant, information from the AB 2588 Hot Spots Program, and other sources, will be used to refine these numbers during the risk management phase.

Up to approximately 320 cancers are estimated per million people exposed to the maximum ambient perchloroethylene concentrations at the City of Industry. Up to approximately 160 cancers are estimated per million people exposed to the maximum concentration at Burbank.

For the combined population of 5.5 million people exposed to perchloroethylene emissions from the eight modeled facilities, over the 70-year lifetime, up

to 17 potential excess cancer cases, that is above those attributed to exposure to background perchloroethylene, are estimated.

Perchloroethylene indoor air exposure is considered important because indoor residential air concentrations have been shown to be consistently higher than outdoor concentrations. The actual levels will vary, depending on the lifestyles and habits of the residents.

In a large California study the mean 24-hour concentration for residential indoor air ranged from 0.34 to to about 1 ppbv. These concentrations were approximately twice the concurrently measured outdoor concentrations. In this study, the maximum indoor air 24-hour concentration measured was about 8 ppbv.

Next is persistence. Reaction with hydroxyl radicals is the dominant mechanism for perchloroethylene removal from the atmosphere, and this removal results in an estimated 150-day atmospheric lifetime; therefore, perchloroethylene is sufficiently persistent to be transported throughout an air basin before it is removed from the atmosphere.

We plan to make the following revisions to the perchloroethylene document before it goes to the Board.

In the Executive Summary, Part A:

Emissions estimates will be rounded and the controversy over the EPA's classification of perchloroethylene will be described briefly.

In addition, the types of facilities modeled for near-source emissions will be described.

In the executive summary, the Health and Safety Code will be more fully referenced when appropriate, and several clarifications will be made for the lay reader.

In summary, perchloroethylene is produced and extensively used in California. Dry cleaners and degreasers are the identified major potential emission sources.

Perchloroethylene is detected in outdoor air, with the estimated statewide mean annual ambient concentration being 0.37 ppbv.

Studies have shown that indoor concentrations are typically higher than outdoor concentrations of perchloroethylene; and finally, perchloroethylene is a federally listed hazardous air pollutant. The California Health and Safety Code mandates that such compounds be identified as toxic air contaminants.

In consideration of the Department of Health Services findings, which you will hear shortly, and the reasons I just summarized, the staffs of the Air Resources Board and the Department of Health Services

recommend that perchloroethylene be identified as a toxic air contaminant.

I will now summarize and respond to the comments we received on Part A.

We received comments from the representatives of five organizations requesting an extension of the public comment period on the perchloroethylene document. They wrote that the comment period we provided did not allow adequate time to review the document, and that it is unfair to give the public ten working days to comment on a document that required over a year to prepare.

The comments were from Mr. Daniel Phelan of Bay Area League of Industrial Associations; Mr. George Laumann, Jr. of California Fabricare Institute; Mr. Paul Kronenberg of Chemical Industry Council of California; Dr. Paul Cammer of Halogenated Solvents Industry Alliance, and Mr. William Fisher of International Fabricare Institute.

After carefully considering their requests for a public comment period extension, we decided not to delay the SRP's discussion of the perchloroethylene report. The public had, and will have, opportunities to comment at the following major milestones of perchloroethylene in the identification process.

First, we issued a public information request for health effects in April of 1986, and received numerous references from the public, including two of the commenters.

The initial perchloroethylene draft report was released for public review in December of 1989 for a 30-day comment period. After receiving numerous comments during this first public comment period, the Department of Health Services preliminary range of risk was revised downward.

Third, in April 1991 representatives of the Department of Health Services and ARB held a conference call with Dr. Paul Cammer, and four representatives from the Halogenated Solvents Industry Alliance. At that time, the DHS discussed in some detail the department's position on the health issues, and it is my understanding that the department's position has not change since the April conference call.

Fourth, the second public comment period, simultaneous with review by SRP members, occurred in May of this year. We are now responding to the comments submitted during that public comment period.

Finally, in addition to the above, public comments on the document may be submitted to the Board any time during the 45-day review period prior to the

Board hearing, which is tentatively scheduled for October of 1991. At the Board hearing, representatives of the ARB, DHS, and SRP will respond to related comments.

In view of the above chronology, we believe that adequate time has been provided for the public to submit comments related to the issues raised in the perchloroethylene document.

BOARD MEMBER GLANTZ: May I just ask one question?

CHAIRMAN PITTS: Yes.

BOARD MEMBER GLANTZ: In one of the comments that came in, they made an issue of fact that at one point you were scheduling a workshop, and that you didn't hold it.

BARBARA COOK: Yes, and we do have that summarized as a particular comment.

Let's see --

BOARD MEMBER GLANTZ: Okay, then you can go on.

BARBARA COOK: It is the next one.

BOARD MEMBER GLANTZ: All right.

BARBARA COOK: We received comments from the representatives of three organizations requesting a public workshop on perchloroethylene.

A perchloroethylene workshop was listed on the August 14, 1990 SRP meeting handout, entitled "Proposed

SRP Meeting Schedule 1990 - 1991" and the three requests were from Mr. Daniel Phelan of Bay Area League of Industrial Associations, Mr. George Laumann Jr. of California Fabricare Institute, and Mr. Paul Kronenberg of Chemical Industry Council of California. As part of streamlining toxic air contaminant identification for compounds under review, and for new compounds entering the process, we planned to have a workshop during or immediately following the first comment period; however, when streamlining was initiated, we were already in the process of revising the perchloroethylene document following the first public comment period.

Therefore, for perchloroethylene, we decided to stay with the original schedule of two written comment periods. We do intend to hold public workshops for future compounds.

A third comment --

BOARD MEMBER WITSCHI: What is the workshop going to accomplish?

BARBARA COOK: The workshop is intended as a means for the public to have access to us in more of a free-flowing conversational type of arrangement.

We usually have a member of the SRP in attendance, although they do not have to comment if they don't wish to. But, this seems to give the public a

feeling that they have more access to the process, and more ability to have their input.

BOARD MEMBER WITSCHI: So, it is not geared to the settling of scientific questions.

BARBARA COOK: No, it is not. It is a discussion.

BOARD MEMBER WITSCHI: Okay.

BARBARA COOK: Our third comment is from Mr. George Laumann, Jr. of California Fabricare Institute.

He commented that the ARB's regulatory application of the DHS cancer unit risk would have profoundly detrimental effects on dry cleaners, including unnecessary public fear and anxiety about dry cleaners, possible law suits, unreasonable toxic air contaminant fees, increased operating costs which would drive some dry cleaners out of business, and no permitting of new dry cleaning plants.

BOARD MEMBER FROINES: May I ask a question about that?

CHAIRMAN PITTS: Certainly.

BOARD MEMBER FROINES: Unless I am mistaken, that is risk management.

BARBARA COOK: That is correct.

BOARD MEMBER FROINES: And, I would prefer that that be left to the risk management phase; therefore, I

don't think this panel should be lobbied on the economic issues.

I don't agree with the separation of management from assessment, but that is the way it is set up, so I think we should maintain that.

BARBARA COOK: That is our assumption also, Dr. Froines.

And, we go on to say that if perchloroethylene is identified as a toxic air contaminant, then these issues that Mr. Laumann brings up, plus the need for an appropriate degree of regulation, will all be considered in the risk management phase of the program.

BOARD MEMBER FROINES: I am saying that I don't think those comments should go to the panel.

BARBARA COOK: Well, the comments actually came to us, to the ARB, and this is our answer.

Basically, that right now we are dealing with identification, and those comments are more pertinent to risk management, as you said.

DR. JOAN DENTON: Dr. Froines, when we initiated the second comment period, we say in those letters to please submit your letters, they will be forwarded to the panel and your individual comments will be responded to at the time of the SRP meeting.

So, we didn't sift through any of the comments.

We just have summarized them, as Barbara is doing. You have received the letters, and we respond to them.

BOARD MEMBER GLANTZ: Yeah, I don't think -- I mean, I agree with John. I don't think we should be -- at least under the current rules -- it is appropriate for us to be dealing with risk management issues.

But, I think that anything people send in should be forwarded. I mean, I think it would be very bad to have the staff censoring anybody's comments. We can choose to ignore them, or to use them, or whatever, but I think they should all come to us.

CHAIRMAN PITTS: Could I just ask a question, although it may be construed as risk management, but it is an indoor exposure.

What information is available, in terms of experimental data? Or, real measurements? What measurements really have been made right in the establishments like the neighborhood dry cleaning establishment, with a very nice guy running it, and his family?

Now, that may even be occupational, rather than, you know, but I am just curious to know what the levels are, to sort of put in perspective what these concerns are that I hear, and also, just in my own personal perspective.

BARBARA COOK: Here in California we don't have a lot of data on what exposures are inside of dry cleaning establishments.

We do have a permissible exposure level put out by Cal-Osha, which is 25 parts per million, and that is a permissible --

CHAIRMAN PITTS: How much?

BARBARA COOK: It is 25 parts per million.

CHAIRMAN PITTS: That is 25 parts per million so, we are --

BARBARA COOK: And, that is their permissible exposure --

CHAIRMAN PITTS: -- and we are talking about an annual exposure in ambient air of .37 parts per billion.

What happens if you multiply 20 parts per million by the number of dry cleaners? Assuming they reach that?

BARBARA COOK: You would get a very high number.

CHAIRMAN PITTS: Okay, and that is an interesting and important point.

BARBARA COOK: Yes.

CHAIRMAN PITTS: Will that number then be dealt with? Specifically, will that be dealt with by the risk management people on the Board when you make that

presentation? Will you make that presentation? With those numbers?

BARBARA COOK: That would be something for Cal-Osha to take up.

CHAIRMAN PITTS: Have they taken it up?

BARBARA COOK: That I am not aware of. They certainly, recently, reviewed their permissible exposure level, and dropped it to 25 parts per million.

CHAIRMAN PITTS: Dropped it?

BARBARA COOK: Yes. It was 50.

But, the important thing, to continue on with exposures at dry cleaners, there is not a lot of monitoring evidence.

There was a report at one dry cleaners -- this is outside of the State of California -- where levels were as high as 1500 parts per billion, by volume. That was like a 24-hour --

CHAIRMAN PITTS: That is 1500 parts per billion, or 1.5 ppm?

BARBARA COOK: Yes.

CHAIRMAN PITTS: Okay. And, was that a 24-hour average?

BARBARA COOK: Yes.

CHAIRMAN PITTS: Okay, and --

BOARD MEMBER FROINES: We have a lot of that

data from the OSHA management information system, and I could print it out for you if you would like it.

We have all of the history of all OSHA -- all of the measurements that OSHA has ever determined since 1979 to the present, so we would just print out dry cleaners and give you the perchloroethylene levels that were found.

BARBARA COOK: Right, well --

BOARD MEMBER FROINES: But, I think -- and the other thing is NIOSH did a control technology assessment a few years ago, and so we have that as well, on dry cleaners, so I think there are a number of them there.

I think, just one comment, when you go from the two-unit system to the single-unit system, when you go from the washer-dryer system, to the one, your occupational exposures decline markedly.

BARBARA COOK: Quite a bit.

BOARD MEMBER FROINES: So, that is an important control strategy.

BARBARA COOK: That's true.

BOARD MEMBER FRIEDMAN: May I just follow up on that?

CHAIRMAN PITTS: Yes.

BOARD MEMBER FRIEDMAN: In your indoor measurements, has anyone ever gone into a closet? Say,

you bring home a batch of dry cleaning, a couple of jackets and pants, and so on, and hang them up in there, what is the level of that closet?

BARBARA COOK: They haven't, to my knowledge, they haven't gone into the closet; however, we do have personal exposure data, where people have been known to visit a dry cleaners during the course of their day, and these people show elevated levels of perchloroethylene exposure. And, it is thought that probably in indoor air the dry cleaning materials that are brought home are a very large source of perchloroethylene.

BOARD MEMBER FROINES: We actually were interested in that question, Gary, and were going to do some studies, and the student who was working with me said that he thought that EPA had already done that, as part of their scheme on that whole environmental exposure assessment study. So, that data may be available.

BOARD MEMBER BYUS: Yes, I remember, actually reading that data somewhere. I had it before, but I couldn't find it, from about three ago, and it was literally just what you said, the taking home of the dry cleaning, taking the bag off resulted in a considerable increase in the air exposure. I don't remember the exact levels, but they were advising you not to -- basically, I

remember this, was to basically air out your dry cleaning somewhere where it would be in a well ventilated area.

BOARD MEMBER FRIEDMAN: Conceivably, if you live, say, in a studio apartment and you get a bunch of dry clean, you could have a fairly high --

BOARD MEMBER BYUS: Exactly, that is what I remember.

CHAIRMAN PITTS: I would like to add to that the ever-present concern of co-pollutants, because you get a lot of formaldehyde that comes on your clothing, and as a matter of fact, just as a little anecdotal episode, when we get our dry cleaning from this friend of ours who is just a block away, we come back and take all of the plastic off -- I do it because my wife is allergic, violently allergic to formaldehyde -- hang it outside -- hopefully under something so the birds don't fly over and make their usual comments on mankind, which I think is fair enough, because I am a bird shooter, too. I hunt, you see, and we are a good target and deserve it.

But, seriously, we do that, we air it out, and it is aired out before it goes into the closet. And, I hadn't even thought about perchloroethylene. My concerns had been formaldehyde.

We have talked to a number of people who are sensitized, and we've talked to experts, particularly

ones in San Francisco, up there, and formaldehyde, and they say do that because the formaldehyde is a problem.

So, I would like to also you to examine this point -- just exactly the point we've made here -- for the record. That is, what happens under different indoor types of exposures, different types of ventilation systems, as it is an important point -- and in the closets -- and also do this for formaldehyde when we've come down, you know, in that area on formaldehyde. Okay, and if you would transmit that back.

And, also, I would like to have -- just for my my own interest, perhaps, well, I think it is of interest to the panel -- could you have someone trace through the steps that will be taken, by whatever particular agencies. Maybe now this is a new role for California EPA, because you look at a large range of situations, but I would like to know how one goes about securing accurate experimental data, easy to do, on dry cleaning establishments? What legal mechanism is involved? What regulatory mechanisms are involved? What scientific? It is not hard to do. You could even do personal. There are a lot of dry cleaners. That point was made by the dry cleaners association, and I am concern about them, and I am concerned that they can keep their jobs. But, I also think it would be important to know what the risks

are involved.

DR. JOAN DENTON: Dr. Pitts, Dr. George Alexeeff was going to address the Cal-Osha question. Would you like him to do it now?

CHAIRMAN PITTS: Would you do that now, George?

DR. JOAN DENTON: Or, when he is up?

CHAIRMAN PITTS: Is this in terms of exposure? Or in terms of impact?

DR. JOAN DENTON: The methods of --

CHAIRMAN PITTS: Exposure now, if it is in terms of effects, then later.

DR. GEORGE ALEXEEFF: It is the process.

DR. JOAN DENTON: The process.

CHAIRMAN PITTS: Oh, all right, then why don't you do that later, then.

Well, Don, do you want to give us this?

DONALD AMES: Good morning. For the record, my name is Don Ames, of the Stationary Source Division with ARB.

Just a couple of comments on risk management, what we would anticipate doing if perchloroethylene is identified as a toxic air contaminant, is to look at it along with a host of other halogenated solvents that have been identified as toxic air contaminants, and to survey the industry to identify trends on use, to look at what

other mitigation measures have been taken as the result of the ozone control program, to see how emissions have been decreasing, look at what else could be done to further lower exposures, and what the incremental costs would be of lowering those exposures further, and what the benefits would be.

At the same time, we would in all likelihood do some more source testing and perhaps some ambient monitoring around some of the major hot spot areas you heard earlier that we expect out of the AB 2588 Hot Spot Program to better characterize public exposures in residences near major sources of perchloroethylene. So, all of those in combination.

We would work together with the criteria pollutant folks, who are also looking at solvent control measures.

At the same time, you mentioned Cal EPA. I would expect there are other factors here that have contributed to lowering the emissions, just in the whole area of hazardous waste handling and disposal costs, and so forth. I think there are a lot of things in place right now that have encouraged source reduction, pollution prevention, by the industry, and I imagine there have been a lot of steps taken to minimize those disposal costs, and to recycle, and so forth.

So, we would go into much more detail then we have in the identification phase, characterizing exposures and control measures that can be taken, and the costs and benefits.

BOARD MEMBER FROINES: I have just one comment about that -- or one estimate. This is a great compound, when it comes to recognizing all of the various uncertainties that go into risk assessment, and it would be terrific if we didn't have to go through all of that, in some ways, which means that people eliminate use of perchloroethylene, which might not be so good for the producer, but for some of the users it might be beneficial.

And, so the question is, what degree do you think there is the potential for substitution of the perchloroethylene?

DON AMES: Well, what I can say is that certainly is one of the things we would look at, is look at the use of less harmful substitute compounds, as a example. We did that with hexavalent chromium used in cooling towers throughout the state. We banned its use because we looked at the technology for substitute compounds, we consulted with the Department of Health Services, and we ended up banning that and looking at less harmful, yet effective compounds, to prevent

corrosion in cooling towers.

Here, we would hold public workshops. It would be an open process. We would hold public workshops with the industry and look at what could be done to either provide less harmful substitutes, or minimize the emissions and public exposure, so that would certainly be part of assessment that we would make before going to our Board with the proposal.

BOARD MEMBER SEIBER: May I ask a question?

CHAIRMAN PITTS: Yes.

BOARD MEMBER SEIBER: We kind of went over pretty quickly the fact that there is a production facility in California. I wonder where it is located? What data there is for people who either work in the facility, or live down wind from the facility?

BARBARA COOK: Well, I can tell you that it is a Dow Chemical facility, and that it is in Pittsburg, California, and we know the production capacity. We don't believe that they operate to capacity each year. That is about all we know about the facility.

BOARD MEMBER FROINES: What about TRI data for that facility? Don't they report emissions?

BARBARA COOK: Yes, but that is their own reported emissions. We've estimated that they could emit up to 66, I believe, tons per year. That is our own

estimate.

BOARD MEMBER SEIBER: So, you are considering that to be minimal compared with the dry cleaning establishments, statewide; although, in Pittsburg, California, it may be a major source.

BARBARA COOK: That is correct. It could be a near source.

BOARD MEMBER SEIBER: I am kind of surprised that you centered on the City of Industry, when you didn't have any data from an obvious population that would be living in and around that Pittsburg facility.

DONALD AMES: I would just like to comment that the Bay Area District is ahead of most other districts in the state, when it comes to the analysis required by AB 2588, and they have their own toxic inventory, and at this point, I don't know the specifics on this facility. I would imagine that the data is already into the Bay Area District, and right now they are working with the manufacturing facility to look at the potential hot spot exposure data. This is a large enough facility, and I would expect that there would be a risk assessment completed within this next year, well in advance of any proposed rule making that we might make.

So, that is one of the very first things we will be doing, is working with the Bay Area, looking at

the quality of the hot spot data, and hot spot emission exposure estimates.

BOARD MEMBER SEIBER: The other comment I had was on the assumption -- as near as I could tell from a quick reading -- that emissions were based on total amount purchased, versus the amount that was either recycled or accounted for after a yearly inventory turned over, and it seemed to me that the trend in the dry cleaning industry has been to recycling their solvents more. I was surprised that there wasn't more recycling going, that the emission maximum was as high as it was estimated to be.

Do you have any comment on recycling, and the trend toward greater recycling?

BARBARA COOK: Yes, I do have a comment on that.

Our data is from 1987, and we recognize that several things have happened since that time, and one of them is that there is more recycling going on. And as I mentioned, if perchloroethylene is identified in the risk management phase, a new emissions' estimate will be done, which will refine our figures.

Okay, if there are no further questions at this time, I will proceed with the comments.

Mr. Paul A. Kronenberg of Chemical Industry

Council of California commented that it is unacceptable that the SRP will not receive oral testimony at today's June 10th meeting, because the scientific basis of the perchloroethylene report is in question.

According to California Health and Safety Code Section 39661, there is no requirement for the SRP to receive public testimony at its meeting. An SRP meeting is not a hearing, but a deliberation among the SRP members on the scientific adequacy of the reports prepared by ARB and the DHS.

In conducting this review, the panel considers all written public comment. The issue of receiving public testimony at SRP meetings has been discussed by the panel members, and it is our understanding that they have decided to base their review on written material, and to not receive oral testimony.

CHAIRMAN PITTS: I should point out that that decision was made quite a few years ago, so this is not a new action on part of SRP.

Yes, Stan.

BOARD MEMBER GLANTZ: And, I would like to just say just one thing about that. At the nickel workshop, which was quite useful in terms of dealing with nickel, this issue came up, and I think that the decision of the panel not to take public testimony, which was made

before my time, was a good one, and I frankly find the written comments much more useful and compelling than oral comments.

The one issue that was raised by a couple of the people who were there though, was that if there is something in the response, in the document prepared by the ARB or the DHS staff, in other words if there is a question about it, they have an opportunity to deal with it. And, the industry people who were there said that that puts them at a disadvantage in not being able to be asked the questions, and that actually struck me as a reasonable point.

And, I was wondering -- I mean we don't need to necessarily deal with it today -- but we might want to consider a slight change in the procedures whereby we could say to other individuals, if they wanted to come to the meetings and make their presence known by signingin, or something, and saying that so and so is available to deal with these aspects of the public comment, should the panel want to ask them a question. That might be worth, at least, trying, in order to give those people a chance to make clarifications.

I don't think having -- I mean, the public meetings I have been to, where you take testimony on technical matters, such as is before us, do turn into a

zoo. I think that the commenters are much better served by having it in writing.

But I think we might want to, at some point, consider allowing them to answer questions, if the questions emerge from the panel.

BOARD MEMBER FROINES: I just want to make one comment --

CHAIRMAN PITTS: Yes.

BOARD MEMBER FROINES: -- following on something Dr. Witschi said earlier, which is that it seems to me that there are complicated scientific questions that come before us, or that arise as the result of these deliberations, and that it seems to me that the resolutions of the scientific issues should be, in part, between the people who want to make comments -- like we have here -- and say, DHS, the scientists from DHS, and there should be forums established to discuss and try and resolve scientific issues, in that overall preparation of the document, trying to resolve scientific issues which will make a better prepared scientific document.

It seems to me that by the time it comes to us we should not be involved in a process like that, because I don't think we are really set up to be, and that I would prefer to see more activity go on earlier, as

opposed to opening this process.

And, the question is, how best do you resolve questions of scientific uncertainty, so that you can go down the road towards identification? And, that is, it seems to me, is the most appropriate place to address it.

I think if you start to open this up, you know, it will become a -- we will lose our quality control role, it seems to me, and I think that that is the danger now.

CHAIRMAN PITTS: I think that both Stan and John have good points.

I think many of us were concerned. I was concerned, and I believe that the industry has legitimate concerns to see the document go out on May 15, and so forth, and then there is the limited period of time. I think it is important, as John has pointed out, to have these discussions with the DHS, and the industry, and the ARB, to be in advance, so that when the material comes to the panel we will have both sides of it. We have the questions. We have the material. And, we have it in advance, at least a week, maybe, some defined period, so that we can look at this and get back, and if some questions arise in our minds we can even go back to the DHS, and through them -- I think it should be through them or the ARB -- through them, go back to the

representatives from industry that have -- that is, their professional people, their experts that they want to bring in. And, I think you are totally right. This should, I think, be done in advance of these meetings.

And, so I think that one of the areas that the panel should discuss with the ARB and the DHS, and get it very clear, is what we think the time line and procedures, clearly spelled out, ought to be, so that in future situations these concerns of industry, and of their experts, and of the panel members and the DHS, can be handled prior to the meeting, but in a very fair and comprehensive manner.

Okay?

Yes.

BOARD MEMBER GLANTZ: Well, I think that there are a couple of things -- I don't want us to get totally side tracked here, but there are a couple of issues.

I think, first of all, and now it is clear that this document is a little bit in the transition from the old process to the new process, but I was impressed that the workshop that we had on nickel, I thought there was a lot of information that changed hands, and the document changed quite radically as the result of it, I think. And, I think that that was a good thing.

While the complaint that the ten days isn't

enough, has sort of become almost routine, and I have to say that the comments that came back were pretty stinging, and I think pretty highly focused on this document, and so maybe you could give them a little more time. But, I think that they may not have gotten a lot of sleep, but there were some pretty strong criticisms that came back on this document, mostly on Part B, we'll be talking about.

So, I don't think we need to extend the period extensively there. I think that is working okay. I still -- and I think we should put this off and put it on the agenda and discuss it another time, and maybe even get some public comments on the idea of how we handle public comments -- but, I still feel that in a way -- well, not in a way -- we are sitting in judgment of these documents and the ARB and the DHS, and if they ever give us anything the CDFA, and I think it is a little bit unfair. I mean, I think it is totally fair for us to say that they should be working with the industry groups, and trying to incorporate the information.

But, I also think it is a little bit unfair to say that any questions -- or if the industry people have had some they have to be filtered through the staff people. At some point, I mean, this is -- John is shaking his head -- but, I mean at some point --

BOARD MEMBER FROINES: I didn't say that.

CHAIRMAN PITTS: He didn't say that.

BOARD MEMBER GLANTZ: -- okay, well then --

BOARD MEMBER FROINES: I think that there should be, to the degree that there are differences of opinion, they should be on the public record, and we should be able to see them.

BOARD MEMBER GLANTZ: Yes, and I think we can.

BOARD MEMBER FROINES: If they want to make further comments for us to respond we should see those.

I just don't want this to become a three-day long process, where take writs, and they will pad us with about 25 people to testify to the material that we have already gone over.

BOARD MEMBER GLANTZ: No, I agree with that. I guess my feeling was much more limited. I do much better with written material, than listening to people talk.

But, my feeling was that it might be reasonable to have people, where if there were specific questions that the panel had, where they might be able to respond to the question about the comments, not just to come in and testify. But, you know, if we were reading through Part C, or one of these letters, and said, "Well, what do you mean here?" I personally think it would be nice to give them the opportunity to answer the question. Not

the right to speak, but the opportunity to answer a question for clarification.

BOARD MEMBER FROINES: It seems to me that we could build that into the process --

CHAIRMAN PITTS: Exactly.

BOARD MEMBER FROINES: -- which is to have a period, short period, in which the panel raised questions that came out of that which they had read, and that from the commenters, and that that could go back and come back in. I think you could build that into the process. And, I think if it is important --

CHAIRMAN PITTS: Well, that is the point I was trying to make. I think it would satisfy both concerns, but, I think that is something that we really should discuss again, the scheduling, timing, when the ARB is on the schedule, and we could build into this -- and we will have to discuss that -- a period where we could exactly, basically, what John is saying, which would make sense.

The comments could come into to you through a mechanism, could come in, come to us, you have your concerns, we have ours, and we can get back and say, we don't understand this, contact so and so. When you get down to the real details, it is possible for someone who is an expert, presented as an expert from one perspective, can come up with a response in a short

period of time. I think we should really think about this.

The idea, I think John Froines and I speak from experience over the dioxin meeting, and people are standing up and reading us the latest thing that just came out of whatever, and were reading this, and then we were being handed statement from the staff that were generated that morning that we hadn't seen before, and I can assure you this was a zoo, and we were inside the bars! That was the problem. And, so I think that we should give this more consideration.

I want to move on, but I would like to have the staff, then, and this is an official request, from what I heard, will the staff come up then with a schedule, and a procedure, and the legal aspects of this, so that we would have something presented at our next meeting, in advance so that we could review it before, which would accommodate this question, and would reflect the concerns that you have heard from us, in a manner that would be effective for all parties concerned, okay?

DR. JOAN DENTON: Dr. Pitts, I was reminded that we do have two more compounds that we are planning on having come to the panel this year, and we are very sensitive to this complaint that we had not given the individuals time enough to respond to this second comment

period.

So, when we anticipate bringing you, at your next meeting would be the time when we would have the discussion of the next document --

CHAIRMAN PITTS: Well, what is the next one, now?

DR. JOAN DENTON: -- the next one would be formaldehyde.

CHAIRMAN PITTS: Formaldehyde, and then butadiene?

DR. JOAN DENTON: Then 1.3-butadiene.

CHAIRMAN PITTS: Right, okay.

DR. JOAN DENTON: So, we may want to maybe discuss with you and the leads, Dr. Froines, about the mechanism before the next panel.

We are already planning on giving the public more time, but the next official panel meeting would be the discussion of the document.

CHAIRMAN PITTS: We have public workshops on both of those.

DR. JOAN DENTON: Right.

CHAIRMAN PITTS: They both have public workshops.

DR. JOAN DENTON: That is correct.

CHAIRMAN PITTS: But, I think, in addition to

the public workshop, that is another issue, and why don't we discuss that then, and set up a schedule --

DR. JOAN DENTON: Okay.

CHAIRMAN PITTS: -- and I am sure we can do one that will be satisfactory to all of us.

BOARD MEMBER GLANTZ: Can I just say one more thing?

CHAIRMAN PITTS: Yes, go ahead.

BOARD MEMBER GLANTZ: I don't see, frankly, what we would gain by adding another kind of question and response period in the written materials. I mean, you might want to give people a little longer for the second public comment period, but you know, I don't think -- the reason that I made the suggestion that I had was because there is a certain dynamic at the meeting, and you know, you do certain preparation for the meeting, and I thought it might be useful to be able to just ask the people some questions.

Now, if the panel thinks that that will become a zoo, I have enough zoos in my life as it is, and that is one thing. But, I don't think that adding in a couple of weeks where the panel would get the document, and then formulate some questions that would go back, and you know, I don't see where that would add anything, quite frankly.

CHAIRMAN PITTS: It is not the document. It is the comments that have come in that --

BOARD MEMBER GLANTZ: Well, I mean the comments on the document --

CHAIRMAN PITTS: -- would mean --

BOARD MEMBER GLANTZ: -- I personally don't think that would really add anything to the process, other than lengthening it, and I think that if you are going to lengthen it a little bit, you would do much better to simply extend the second public comment period a little bit more, rather than add, because if we add a week for this to go back and forth, then the people are going to say, well, a week isn't enough time to go back and forth.

You know, there is already informal mechanisms in place, at least I found in dealing with nickel, that you know if there are some things in the public comments that come up that you want to clarified, well, I just call up the staff and ask to get them clarified, and they did. So, I don't think we need to have any formal -- if that is the model that people want to work to, I don't think we need to have any formal change in procedures.

BOARD MEMBER FROINES: I was just responding to the subject that you raised the question about.

BOARD MEMBER GLANTZ: Okay, well, maybe we

should just -- I think this is going to just make it more complicated.

CHAIRMAN PITTS: Well, I think there is an important issue here that is worth discussion.

I think we all feel -- I am not going to just speak for I. I think I can speak for the whole panel, that we all want to feel that industry, representatives of industry, have a fair shake all the way across. We want to feel that they are exposed to the latest information that is coming out, published and unpublished, some of which -- although we really have to respond to published information in our peer review journals, but we are available to read material in reports, and so then I think it is an important point, that we handle this in a manner that all involved do have full input to this. That is more important, I think, than two weeks more in its coming out.

So, we will have to think about this. We will think about this and give it our thought, and then we can informally come up with something, with your suggestions as to how it ought to be done, and how it might modify the program to some degree.

And, I want to be sure that it is legally correct, and that all in turn have their fair share of input into this, as critical decisions are being made,

and I think we want to be sure that we have all of the input that we can.

Would you care to go ahead now with your --

BOARD MEMBER FROINES: May I say one thing.

CHAIRMAN PITTS: Yes, go ahead.

BOARD MEMBER FROINES: Can I just ask that we talk about formaldehyde at the end of the day, because I just sent a note to George that we have to take up proliferation in considering the risk assessments of the scientific issues that he said might take two months to complete. And, so at the end of the day if we could talk about that.

DR. JOAN DENTON: That would change the schedule.

BOARD MEMBER GLANTZ: I would like to make a comment, to suggest that in response to concerns expressed by the industry, it might be worth getting their -- having the staff get some input, because if you apply the constraint that we just don't want to have a general open public hearing, but we want to give, you know, to make sure the information is transmitted as effectively as possible. Do they have any suggestions of ways that could be done without seriously slowing the process done. Maybe get some input from there, too.

DR. JOAN DENTON: Well, one thing, Dr. Glantz,

is that the effected industries do change with each compound --

BOARD MEMBER GLANTZ: Oh, that is true.

DR. JOAN DENTON: -- and we don't have the same respondents, although the HSIA we I have seen before, but the effected industries are going to change --

BOARD MEMBER GLANTZ: That's true.

DR. JOAN DENTON: -- and some of them --

BOARD MEMBER GLANTZ: Maybe we should just leave it alone.

DR. JOAN DENTON: -- are more familiar, some of them are less familiar with the process.

We are, though, planning on having a longer second comment period, though.

BOARD MEMBER GLANTZ: How much longer were you thinking of extending it?

DR. JOAN DENTON: We were thinking in terms of three weeks to four weeks.

CHAIRMAN PITTS: I think that within that framework we can probably accommodate.

Okay, I think we should move on now, in the interest of the fact that I have just heard about formaldehyde, which is an important question and should be discussed. We ought to probably move along, and we will put that on the agenda, definitely.

Okay.

DR. JOAN DENTON: Barbara will continue.

BARBARA COOK: Yes, I'll go on with the next comments.

We received related comments from Dr. Paul Cammer of Halogenated Solvents Industry Alliance, and Mr. William Fisher of International Fabricare Institute regarding our position that as a federal hazardous air pollutant, listed under Section 112 of the 1990 Clean Air Act, perchloroethylene is required to be identified as a toxic air contaminant pursuant to Section 39655 of the California Health and Safety Code.

Our legal counsel, Kathleen Walsh, will respond to this issue.

COUNSEL WALSH: I wanted to point out, initially, that the language of the statute is very unambiguous on this point.

It states that substances that have been identified as hazardous air pollutants, pursuant to Section 7412, Title 42 of the United States Code, which is Section 112 of the Clean Air shall be identified by the state board as toxic air contaminants.

Typically, when you have legislation that is clear on its face you don't look behind it to make different interpretations of the language. Nevertheless,

when Congress amended the Clean Air Act last year, we considered the effects of the automatic listing of the 189 compounds on this program.

We considered, specifically, the argument that had been presented by the two commenters, and rejected it for a specific reason. Back in 1983 when AB 1807 was initially enacted, EPA was charged under Section 112 of the Clean Air Act with identifying hazardous air pollutants, and at that time they had identified approximately eight compounds.

However, the anticipation was clearly that EPA would continue that process and that compounds would be added to the list over time. There is nothing in the language of the Section 39655, that I read to you a moment ago, that indicates that the legislature, the state legislature, intended to make a distinction between compounds that were identified when 1807 was enacted, and compounds that were identified subsequent to that time.

The other factor that we considered is that when Congress acted last year to add the 189 compounds to -- just list them specifically in Section 112, they were doing that in large part because EPA had not moved forward and acted more quickly to enlarge the list of hazardous air pollutants.

So, what Congress was doing was really very

much in line with what our legislature anticipated happening back in 1983. Nobody may have expected that there would be 189 compounds on the list at this date, but certainly the expectation was that that list would be enlarged. And, there really is no way to make a distinction at this point om time, and given the very specific and unambiguous language of the state statute, we don't see that there is any other interpretation that our Board can take.

BARBARA COOK: Thank you, Kathleen.

CHAIRMAN PITTS: Thank you.

BARBARA COOK: Finally, we received three letters commenting on the EPA controversy regarding the classification of perchloroethylene as a carcinogen.

The Department of Health Services will address the EPA's classification of perchloroethylene, and respond to other comments about the health assessment.

Before we proceed to the DHS' presentation, I would be happy to answer any questions concerning Part A of the report.

[No Response.]

CHAIRMAN PITTS: Are there any questions for the staff?

I have no questions.

Thank you very much.

BARBARA COOK: Okay, thank you.

CHAIRMAN PITTS: We'll move on to Dr. Alexeeff.

DR. GEORGE ALEXEEFF: I am George Alexeeff, California Department of Health Services, and with me is Dr. David Lewis of the department, as well, and he assisted in preparing the report, and I just want to mention at the beginning, although it is clearly stated in the report, that much of the work was initially done by Drs. Ken Bogen and Thomas McKone of Lawrence Livermore Lab, in analyzing the harmful kinetic metabolism of the perchloroethylene, and we used their analysis and incorporated it into this report.

BOARD MEMBER FROINES: What were their names?

DR. GEORGE ALEXEEFF: Excuse me?

BOARD MEMBER FROINES: What were their names?

DR. GEORGE ALEXEEFF: Ken Bogen and Tom McKone of Lawrence Livermore Laboratory.

I'll first summarize the report, and then discuss the comment that we have received.

Perchloroethylene readily diffuses into the blood and into the adipose tissue where it accumulates due to its relative stability and slow metabolism. The main metabolic pathway for perchloroethylene appears to involve its oxidation by cytochrome P-450. In humans, a mass balance of perchloroethylene absorption and

elimination is not available.

Trichloroacetic acid compounds account for 60 to 80 percent of the metabolites of perchloroethylene in rodents. This drops to four percent measured in humans, with 20 to 60 percent of the dose being unaccounted for in the human studies. Thus, while the rodent data are well defined, the human metabolic data are incomplete. Models describing the kinetics of perchloroethylene have been developed. The primary uncertainties in the models are identification of the toxic metabolite and the amount of metabolites produced by humans.

Perchloroethylene has moderate toxicity, with the liver being its principle target organ. The products of perchloroethylene metabolism are thought to promote liver toxicity.

Inhalation exposure of pregnant rodents to 300 parts per million produced maternal toxicity and fetal toxicity manifested as developmental delays and altered performance in behavior; however, perchloroethylene is not considered to be a teratogen.

The no-observed-adverse-effect-level for chronic inhalation in rats was reported to be 70 parts per million; however, a NOAEL for mice has not been established.

BOARD MEMBER SEIBER: Is that 70 parts per

million or billion?

DR. GEORGE ALEXEEFF: Per million.

BOARD MEMBER WITSCHI: What is the definition of no effect, after all some of the rats had cancer --

DR. GEORGE ALEXEEFF: Right, so this would be for --

BOARD MEMBER WITSCHI: So, what is the NOAEL, then?

DR. GEORGE ALEXEEFF: -- this would be for a noncarcinogenic inpoint, of liver toxicity.

BOARD MEMBER WITSCHI: Oh, I see.

DR. GEORGE ALEXEEFF: Humans have shown signs of liver toxicity after chronic exposure of 200 to 400 parts per million.

The California Department of Health Services' staff do not expect noncarcinogenic adverse health effects to occur from acute or chronic exposure to ambient air concentrations; however, 24-hour maximum average concentrations of perchloroethylene measured in urban areas were approximately five parts per billion, which is the EPA reference dose.

Perchloroethylene increased the incidence of hepatocellular carcinoma and adenoma in laboratory mice after oral and inhalation exposure, and mononuclear cell leukemia in rats after inhalation. Rats also had an

elevated incidence of kidney tumors, although it was statistically significant.

Epidemiological studies have provided some indication that use of dry cleaning solvents poses an increase risk to cancer for exposed workers, however, investigators were unable to differentiate among the exposures to various solvents, and possibly confounding factors, such as smoking and low-socioeconomic status.

The International Agency for Research on Cancer reviewed the carcinogenicity data for perchloroethylene and placed it in Category 2B, a possible human carcinogen, based upon sufficient evidence of carcinogenicity in animals, and inadequate evidence in humans.

Staff of the USEPA has recommended PCE be placed in Category B2, that is, a probable human carcinogen; however, the EPA's halogenated solvent sub-committee to the Science Advisory Board has stated that perchloroethylene is somewhere between a possible and a probable human carcinogen. The classification has, and is undergoing, a considerable debate at EPA and has not been finalized over the past five years, thus its classification as a C carcinogen made in 1985 still stands.

The Department of Health Services --

Yes.

BOARD MEMBER WITSCHI: What did EPA say? A C?

DR. GEORGE ALEXEEFF: A "C", in 1985. That was prior to the inhalation studies.

BOARD MEMBER WITSCHI: Um-huh.

DR. GEORGE ALEXEEFF: So, that still stands.

BOARD MEMBER WITSCHI: What do they say now, today?

DR. GEORGE ALEXEEFF: Now?

BOARD MEMBER WITSCHI: Today.

DR. GEORGE ALEXEEFF: As of today it says C, but there are staff reports recommending that it be changed to B2.

BOARD MEMBER WITSCHI: But, if it is that now, how do we get the document that has the B2?

DR. GEORGE ALEXEEFF: Okay, the findings, yes, those will have to be -- you are referring to the findings?

BOARD MEMBER WITSCHI: Yes.

DR. GEORGE ALEXEEFF: Those will have to be changed.

BOARD MEMBER WITSCHI: This has been all of the time, you know, consistent in those reports and all of the documents --

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER WITSCHI: -- it is B2 --

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER WITSCHI: -- and consistent with what has been raised is a C, or something like this.

DR. GEORGE ALEXEEFF: Well, what happened was in all of the EPA's reports it referred to it as a B2, and --

BOARD MEMBER WITSCHI: Then, where from do you know that it is a C?

DR. GEORGE ALEXEEFF: Well, this year, there was a lawsuit against EPA from the industry, the dry cleaning industry, and they were able to show the court that the EPA has not officially endorsed the B2 status that has been stated by the staff, and so it was delayed earlier this year, the statement that it was a B2 carcinogen was deleted from the federal register.

So, now it reverts and is considered a C until the EPA -- head of the EPA, Reilly, makes a decision.

BOARD MEMBER GLANTZ: Well, the report -- that is not the impression you get from reading this report. I mean, reading Part B and the Executive Summary, I came away very confused by the public comments that came out of this.

DR. GEORGE ALEXEEFF: That is correct.

BOARD MEMBER GLANTZ: The document makes it

sound like it is a B2, and they were thinking about maybe down grading it to a C, so I think the documents needs some fairly major rewriting to make that point.

DR. GEORGE ALEXEEFF: We will make, in my comments I will indicate, and we will change that.

BOARD MEMBER WITSCHI: Well, excuse me, but really what bothers me is that thing is a draft, as a document, and it is a 1991 meeting, that it says there, and that bothers me, and you tell us in this draft it is a C Group. That is bothering me.

BOARD MEMBER BECKER: And, I think that I was most confused by that because the commenters were very strong about that, very pointed in their remarks, and I guess that takes me back to what we were talking about before, that at least I wasn't clear in the information that was supplied to me that there was that much controversy, and then to have it come from the commenters who came to a very pointed discussion, it was most confusing.

There was one thing that I was going to suggest before, the lead person probably, by having a chance to get into that would have known that information before, and clearly clarified the preliminary findings, and everything else, so that it wouldn't just come to us at the last minute. I did find that very confusing.

DR. GEORGE ALEXEEFF: It was only clarified to us in the last comments that came in from industry, in this past ten days --

BOARD MEMBER BECKER: So, you didn't know about it, either.

DR. GEORGE ALEXEEFF: -- so we are only changing it at that point, and we've called numerous staff people in EPA to confirm to make sure that it is correctly a C, so as a result, later on, I will indicate what changes we'll make to clarify that.

But, it wasn't made apparent to us, and as I will mention later, part of it is because EPA staff are continuing along in their regulatory actions acting as though it were a B2 --

BOARD MEMBER WITSCHI: Well, but then --

DR. GEORGE ALEXEEFF: -- and that is what was confusing to us, because the regulations say we are suggesting, which was implying to us that it was a B2. It was only earlier this year it was officially deleted, and that wasn't pointed out to us, clearly until this last comment period.

BOARD MEMBER WITSCHI: So, it is a problem of the EPA, the problem is their staff doesn't know what the other half is putting into the Federal Register.

DR. GEORGE ALEXEEFF: That is possibly a

concern here, yes.

BOARD MEMBER FRIEDMAN: On a related point, on the bottom of page 415, the message that you gave that IARC regards this as a possible carcinogen does not come through clearly. I keep reading about inadequate evidence there, and I think you should, you know, I think that is an important criteria for us to consider too, what IARC's rating is, and it doesn't come through there, where they say it is a possible carcinogen.

DR. GEORGE ALEXEEFF: Where is that?

BOARD MEMBER FRIEDMAN: The bottom of page 415.

DR. GEORGE ALEXEEFF: Oh, I am sorry, yes, that is because it is discussing strictly the human evidence, which was inadequate. The animal to evidence was sufficient.

BOARD MEMBER FRIEDMAN: I know, but I think --

DR. GEORGE ALEXEEFF: Okay, we could add a sentence in there to clarify that, in terms of mentioning its overall classification, as well as this specific human classification.

BOARD MEMBER FROINES: Well, let me make a comment about that, because when this legislation was passed, it was passed in part because the federal government was not moving as rapidly on the issue of toxic air contaminants, as the state legislature, and

others in this state felt was appropriate. This legislation passed precisely because of the failure at the national level to address the issues of toxic air contaminants.

And, I have felt for a long time that what happens is that we see up front the comments, what IARC has said, or what EPA has said, or what some other authoritative body has said, and I think that we should determine what we think, is the first thing. That is the first thing we should do. We should say the state has done the following evaluation, and so on and so forth.

And, that is the way the state legislature intended us to do it, and I think that we should have a box then, that you could outline, so it can become very clear, and says: and also, this is what other agencies have done in this regard. And, then you don't have to go looking for it the way Chuck Becker describes it as looking -- or Gary describes it in 415 -- but have it in one well-defined spot.

But, it still seems to me, and this is the other point I am making, this is your evaluation. This Part B is a better evaluation than has ever been done by EPA. And, so we shouldn't, in a sense, get tied up into looking at the issue of what EPA is doing, and the controversy between B and B2 and C, and lose track of the

quality that went into this piece of work. EPA has never done anything at this level sophistication, and so I think that we need to keep in mind what we are all about in this process.

BOARD MEMBER WITSCHI: Yes, but there is this one point that I would like to make.

I don't know about EPA, but I think it would be asking too much to comment on the deliberation of carcinogens the way IARC does it. Because, what IARC does goes back to the actual data, and it looks at study for study, individual, when it was well conducted, and all of these kinds of things, the patients, the number of animals, whether the data are older.

And, to redo this, I think, would be counterproductive to some extent. Besides, I don't think you would have the expertise to do this. IARC works on experts from a world-wide basis, to exactly analyze the studies which are conclusive, and they toss out the studies that are not conclusive.

BOARD MEMBER FROINES: I agree with you. I agree with you 100 percent. In fact, I have always felt that the state should not try and -- the state doesn't bring together the same quality of science as IARC chemists do.

So, don't misunderstand. I agree 100 percent

with what you say. But, in this case, we are dealing with an issue that IARC doesn't address, that is pharmacokinetic modeling and risk assessment. And, here, the issue of how we assess the risk, and the complexity of that process is something that is uniquely done here. But, aside from that I would agree 100 percent with you. I don't think we should put ourselves in that place of IARC.

BOARD MEMBER SEIBER: Jim, can I make a general comment?

CHAIRMAN PITTS: Yes.

BOARD MEMBER SEIBER: This is coming from a chemist and not a toxicologist, so you have to appreciate where it is coming from, but as I read over health data a couple of questions occur to me -- maybe you are going to get to this, George -- but most of your epidemiological data, which to me is really the thing I am looking for, is what's happened in humans after known exposures, is from the dry cleaning industry and related things, but chlorinated solvents have been used heavily in the chemical and metal industry for years and years, to the point where, having worked in Dow Chemical I can tell you quite frankly that the exposures were massive, to the point where you had jaundiced workers, and things of type, so there must be some epidemiological data that

says --I can't believe that it is at a "possible" or "probable." It seems to me that question ought to be settled by now, after all of these years for perchloroethylene.

BOARD MEMBER FRIEDMAN: But, you know, judging from some of the reports about the dry cleaning industry, then wouldn't it also be true of the chemical industry, that you can't find a group that was just exposed toperchloroethylene. They were exposed to a lot of different solvents, and you don't know how to decide which one is causing the problem.

BOARD MEMBER SEIBER: That is probably true, but even in the chemical industry, you make one compound in this section of the plant, and you make another one over here. There ought to be some kind of reasonable estimate on what the largest exposure was, at least, say for a six month or year period for these people.

I have a hard time accepting it, the lack of information.

DR GEORGE ALEXEEFF: Well, we wish we had more information as well. We just try to report everything that we have found, and that other agencies have found.

BOARD MEMBER FROINES: I will say that I agree with Chuck Becker. This has been confusing, and I actually asked George, as a lead person on this issue

sometime ago, and I was noticing that this document is actually the best thing that I read, and it came from the industry, but it finally clarified the issue. This is the Inside EPA Weekly Report, and it is dated May 31, 1991, and it is too bad that we didn't have something like this until now, because this actually clarifies the issue for me, anyway, and that -- but it is a resent, this article at least is resent, suggesting an issue, still recent in some respect.

BOARD MEMBER GLANTZ: Well, in any event, I think you need to adjust the document accordingly. It might even be worth including that, a reprint of that. I agree with John, that finally clarified the thing for me. It might even be worth including that in the document, itself, in an appendix.

DR. GEORGE ALEXEEFF: Sure, we'd be happy to.

That is in part what clarified it for me, as well. I am sorry it came out it in May.

In any case, the --

BOARD MEMBER GLANTZ: So, just for the record, it does show that we do read the public comments.

DR. GEORGE ALEXEEFF: Oh, I know you do.

The science advisory panel for Prop. 65 also voted to list tetrachloroethylene as a chemical known in the state to cause cancer in 1988.

Perchloroethylene has generally produced negative results in genotoxicity assays, although a few positive responses have been reported, but at least four of the presumed metabolites of perchloroethylene have shown evidence of genotoxicity. These responses indicate that perchloroethylene, itself, or more likely some of its metabolites are potentially genotoxic.

California Department of Health staff have found no evidence of a carcinogenic threshold level, and the staff recommends that perchloroethylene be considered as not having a threshold for carcinogenicity.

Results from the 1986 National Toxicology Program inhalation studies in mice and rats were used as the basis for estimating the carcinogenic risk for perchloroethylene to humans. The department staff used the metabolized dose, adjusted to continuous life time exposure to calculate the carcinogenic potency of perchloroethylene.

There are several uncertainties that accompany the metabolized dose adjustment. The metabolized dose approach, as it has been applied to perchloroethylene, assumes that the oxidative metabolism leads to the production of carcinogenic metabolites, but the ultimate carcinogen has not been well characterized.

A mutagenic glutathione conjugate has also been

identified. A metabolism of perchloroethylene has not been well quantified in humans. The residual perchloroethylene that could be metabolized to trichloroethylene compounds over time, or to nonchlorinated metabolites, such as carbon monoxide or oxalic acid. This relates to the 20 to 60 percent of absorbed human doses unaccounted for, and would be not possible to determine where this unaccounted for dose went without using radio labeled compounds.

Data on the amount of perchloroethylene metabolized at ambient concentrations are not available, but several studies indicate that perchloroethylene metabolism increases as concentration decreases. Department staff believe that these concerns regarding metabolism can be taken into account for the most part by assuming a human metabolic rate of 25 percent, as proposed by Dr. Dale Hattis as an upper bound.

The upper range of human metabolism at low concentrations has been estimated to be as high as 73 percent.

Pharmacokinetic models generally do not account for individual differences in metabolism and storage. A high variability of body burn of perchloroethylene was found dependent upon age, sex, exercise, work load, body mass, adipose tissue mass, pulmonary dysfunctional

states, and individual differences in the intrinsic capacity to metabolize perchloroethylene.

Induction of perchloroethylene metabolism by diet or lifestyle factors can also increase the variability in humans. Human variability in perchloroethylene metabolism and interspecies differences could be accounted for through the incorporation of the surface area correction. The department staff have chosen to utilize the metabolized dose approach with the surface area correction.

For the low dose perchloroethylene risk assessment, the Crump multistage model was applied to the data of both rats and mice from the 1986 studies, using five different pharmacokinetic models. The upper bound of extra cancer cases predicted from a lifetime exposure to one part per billion of perchloroethylene was estimated to be 2 to 72 x 10 -6. Considering the quality of the studies, and the importance of incorporating a 25 percent estimate of metabolism in humans, the best value for the upper 95 percent confidence interval was chosen to be 54 x 10 -6 per part per billion. This compares with the current draft 1986 EPA estimate of 6.5 x 10 -6, which assumes a 4 percent rate of metabolism in humans.

Utilizing this approach, the risks for humans are lower than for rodents. That is to say that

perchloroethylene is less potent for humans than for rodents, using this approach.

Higher risks can be obtained with other metabolized dose approaches, and the risk could be increased three-fold --

BOARD MEMBER WITSCHI: Excuse me, George.

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER WITSCHI: Would the rodent state, or potency there, wouldn't this come from the liver tumors in mice?

DONALD AMES: Yes.

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER WITSCHI: Then this might explain why for humans it comes out lower than for rodents, you know, because of their -- you look at one of their mice with a dirty look, and she develops liver cancer.

DR. GEORGE ALEXEEFF: Well, it is also, if you look at the other, the leukemia data in rats, it is consistent with that as well, in the same range.

BOARD MEMBER WITSCHI: Well, if you treat the rat shabby then she gets leukemia.

DR. GEROGE ALEXEEFF: Well, we are just using the best data that we have.

Let's see, so based on the Department of Health Services potency evaluation, and the annual average

developed by the Air Resources Board of .3 parts per billion in California, an upper limit of 600 additional lifetime cancer cases are estimated in the 30 million residents of California. The calculations represent the upper range of plausible excess cancer risk. The actual risk, which cannot be calculated, may be insignificant.

Based on the finding of carcinogenicity and the results of the risk assessment, the staff for the department concludes that perchloroethylene is an air pollutant, which may cause or contribute to an increase in mortality, or in serious illness, or which may pose a present or potential hazard to human health.

I want to make some comments on the earlier draft. As indicated previously by the Air Resources Board, a draft was released in December 1989, and that original draft, although it referred to to pharmacokinetic analysis it used the applied dose for the generation of the risk assessment number. And, in part, and in response to the comments submitted to the department, and also in the newer data that came out which put into light the uncertainty revolving around the metabolism data, we felt we were able to come up with a risk number based upon the pharmacokinetic data.

Also, in response to the industry comments, the earlier Gavage study of the National Cancer Institute for

Mice was eliminated from the range of risks because of -- well, for one, the major reason is that the inhalation studies are more appropriate, and there has always been concern of corn oil dosing by Gavage.

One thing that I wanted to point out is there is a discrepancy which wasn't picked up in the comments, but we had noticed in reviewing everything, and that is that the document Part B clearly states the risk that was reduced by going from an applied dose approach to a pharmacokinetic based approach, but in the response to comments there was an error, and implies that the reduction was 15 fold and it was not that great. It was more on the magnitude of 2 to 3 fold for the specific best estimate. So, that will be corrected in the addendum. The document was correct in its discussion, but in the response to comments an error was made in there, so I wanted just to clearly state that.

Now I wanted to discuss the more recent comments that were submitted. We have three, from three different organizations.

The first one is from the California Fabricare Institute, and the comment is that the department concluded that a best estimate of upper bound risk of 8 x 10 -6 per microgram per cubic meter is over 13 times higher than the EPA unit risk estimate of 5.8 x 10 -7,

used by air districts in California. The EPA, and the Department of Health Services use the same data in arriving at the different estimate.

Well, there is one slight clarification which needs to be made, and that is that the number currently being used in California is the number based upon an EPA number based upon Gavage studies, because that is the officialized document, just as the C classification is the official classification. The official number for EPA would be the report that was accepted.

The draft report, which uses the inhalation studies and proposed B2 classification, has never been finalized by EPA. So, in the current number that is used in California is the Gavage number -- or a Gavage number developed by EPA.

The actual difference between the EPA inhalation number and the department inhalation number is 8 fold, as opposed to 13 fold.

Since the 1986 draft EPA risk assessment was developed, several articles have been published indicating the uncertainty involved in metabolism and pharmacokinetic data. The articles include Hattis, et al., 1987; Hattis, et al., 1990; Bois, et al., 1990; and Bogen and McKone, 1987.

The DHS document incorporates the scientific

data for these studies in its risk assessment. These studies indicate that metabolism perchloroethylene in humans may be as high as 73 percent. This new data -- or new analysis is clearly summarized by Bogen and McKone in 1988, who stated that "taking ... uncertainty into account, we estimate the [fraction of the maximum plausible metabolic rate] to be between 5% and 65% ... It has been inferred from [human] experimental studies that [the metabolic rate] range is from 2 to 4%, whereas we, using an analytic PBPK approach..." that is physiologically based pharmacokinetic model approach, and other investigators using a numerical PBPK approach, ..."have shown that the [metabolic rate] may actually be greater by a factor of 10-20."

For this reason, the Department of Health Services chose 25 percent as its metabolic rate for humans in contrast to the 4 percent rate assumed by U.S. EPA. And, because of this difference the DHS estimate is eight-fold higher.

The next comment is that the upper-bound unit risk estimate suggested by the Department of Health Services implies that dry cleaners, the individuals in dry cleaners, exposed to 25 to 50 parts per million during their working life time will have an excess cancer incident of 225,000 to 400,000 per million, and there is

no evidence in existing working populations that any excess cancers are occurring among the dry cleaning workers, let alone 225,000 to 400,000 per million.

In our responses, that estimates based on TLVs do not address the actual risks, since the mean-exposure concentration is unknown, and is likely to be far below the TLV. The comment does not indicate how the estimates were derived in its comment, so we can't specifically determine if these number were correct.

As indicated in the summary, and in Section 4 of our document, there is some indication that dry cleaning solvents pose an increase cancer risk, although a specific solvent could not be identified, and confounding factors could not be eliminated. The assumption that all workers that have been exposed to perchloroethylene at the TLV is unrealistic,. since worker histories, job classification, and solvent use have changed over time.

If we focus on a specific study, that of Brown and Kaplan, where there is exposure data in the dry cleaners, we find that the risks found in the study are not inconsistent with the risks predicted in the Department of Health Services analysis.

BOARD MEMBER WITSCHI: Can I make a comment, George?

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER WITSCHI: I hate to tell you, but what you just said, that is going to come up as in the 1,3-butadiene when somebody points out that if you go by the risk assessments derived from animal studies, how come there is absolutely no evidence among older worker that there is an increased risk?

So, this is something, maybe a bit more general, you know, you might want to consider because with many of those things, if you develop a risk assessment then somebody is prone to take you up and question you with it. By going and saying, yes, if your risk assessment is correct then we should. But, they are not going to find it. It happened to us with trichloroethylene. It happened to us with 1,3-butadiene.

If you apply the risk assessment as derived from the animal studies in the real world it just is not there.

DR. GEORGE ALEXEEFF: That certainly is, in terms of applying it to go the TLV, and assuming the complete worker --

BOARD MEMBER WITSCHI: Whatever measure? The TLV? Or measure of concentration?

CHAIRMAN PITTS: Would you please get on your microphone.

BOARD MEMBER WITSCHI: It is kind of something to think about.

DR. GEORGE ALEXEEFF: Yes, it definitely is. That is one of the -- we would all like to, I think, rely on the human data, but the studies aren't there, as far as we can tell, that analyze the data.

BOARD MEMBER GLANTZ: But, you know, George, this, of all of the comments that came back, this was the one that bothered me the most, because it seems to me that what they are basically saying is that if the risk estimates -- I mean, I agree that there are problems with the human's data in this case. I mean, I think you have done a nice job of describing all of the confounding variables, and the difficulties of interpretation.

But, I think that the point that the commenter is coming back with is this thing, okay, if we take your risk number and just apply it to the occupational exposures, we ought to be seeing some large number of cases.

I mean, I don't know where they got that number, either. I think it was 980,000 per million, which seems like an awful lot. But, I mean, there ought to be a lot, and you haven't convinced me that you really have addressed the question of why -- it is almost like if the animal studies are right, why didn't you find

something in the human data? It is sort of the other way around. I mean, you say, you go out and you do the epidemiological studies, and there are a lot of reasons that make it hard to interpret them, but it seems what they are saying is that there should have been so many deaths that you shouldn't have had any trouble interpreting them.

DR. GEORGE ALEXEEFF: Well, actually I was going to address it further, getting into the housing and solvent industry comments, because they explain how they make their calculations --

BOARD MEMBER FRIEDMAN: I just have one question.

BOARD MEMBER GLANTZ: Okay.

DR. GEORGE ALEXEEFF: -- but, I could jump to it right now, to lay it to rest.

BOARD MEMBER GLANTZ: Well, whatever, okay.

BOARD MEMBER FRIEDMAN: Would you --

DR. GEORGE ALEXEEFF: All right.

BOARD MEMBER FRIEDMAN: -- because it would fit in quite well with this, if you could.

BOARD MEMBER BYUS: Before you do that, let me just ask you a question.

Is that okay?

CHAIRMAN PITTS: Yes.

BOARD MEMBER BYUS: Does the metabolized doses, does the metabolism saturate at some low level? It seems to me, as I recall, and I actually read part of Hattis' original document that he made.

But, if the metabolism saturates, then you can extrapolate into these high levels and get these high incidences, but you are not going to have any more carcinogenic metabolites, and that is why it wouldn't occur.

DR. GEORGE ALEXEEFF: That's right, and it does saturate --

BOARD MEMBER BYUS: It is only linear in the low, low, low, levels, if the metabolism is saturating.

I don't know where exactly metabolism saturates, you see. You are only going to have so much carcinogenic metabolite, up to a certain dose, they you are not going to have any more.

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER BYUS: No matter how much perchloroethylene you inspire.

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER BECKER: But, they can't know that when they don't know which metabolite caused it --

BOARD MEMBER BYUS: Well, I mean, that you can

go --

BOARD MEMBER BECKER: There are only so many --

BOARD MEMBER BYUS: Well, that is true --

BOARD MEMBER BECKER: -- that the spread there is so tremendous --

BOARD MEMBER BYUS: -- but, you can make that -- I mean, I am just trying --

BOARD MEMBER BECKER: -- you know, and I think that --

BOARD MEMBER BYUS: -- and that might -- I mean I was just asking if that could account for it.

BOARD MEMBER BECKER: -- it is disturbing in a way, but isn't dioxin the same sort of thing where it is incredibly doing all of these awful things, and clearly causing the same kind the problem in laboratory animals, guinea pigs, and others, and yet when we get to the humans, who have had exposures, and invasive, and we follow them, as the people as in Nitro, West Virginia, when we reviewed that, and maybe you don't see that either, so I think that that is usually chalked up to PCE's variabilities, and with these unknowns, I am not so surprised that that argument is there.

I think that goes with the territory, at least the way I've looked at this territory before, with dioxin being a better example, where you can measure internal

markers, windows, and that sort of stuff.

But, it is disturbing because the argument -- he makes a very strong argument here saying, well, look, my God, at 50 ppm, or 25 ppm, we should have all of this cancer which would have been easily detected, and the same argument would be for dioxin, as well.

BOARD MEMBER WITSCHI: Well, then, those considerations came up at the recent meeting by the Health Effects Institute, and somebody had to comment on what this means, this discrepancy between estimates, and what we really see, huh? Other work may be -- that is the foot in the door, to crack open the risk assessment problem.

DR. GEORGE ALEXEEFF: I's sorry, I didn't quite understand --

CHAIRMAN PITTS: Yes, you need to be on your microphone.

BOARD MEMBER WITSCHI: It might be that this is now -- this was disputed then, and we now have finally cracked open the door --

DR. GEORGE ALEXEEFF: I see.

BOARD MEMBER WITSCHI: -- and what he clearly meant to say is that maybe the way we look at risk assessment, or the data over the last ten years, and so it might undergo -- might be in need of some rethinking.

DR. GEORGE ALEXEEFF: Well, it is clear --

BOARD MEMBER WITSCHI: That is what I meant when I forewarned you.

DR. GEORGE ALEXEEFF: -- no, and I think you have a good point, and making it a more global statement, the previous cancer guidelines that we go by in the state, have very little discussion on using epidemiologic risk assessment information for risk assessment, and that is undergoing revision now, as we had a presentation a couple of meetings ago. And, I think the same holds true for EPA, where the point is that the animal numbers have been very -- the animal numbers have been incorporated into the risk assessment process, and how to use the study, and that kind of thing. I think, previously, there has not been much work on using the epidemiologic evidence for the studies, because of the exposure data is so poor.

But, I think that one, as the exposure data is becoming better, or other methods are being developed in epidemiology to somehow get around the issue, then maybe, you know, we could get a better handle on the risk. But, part of the problem is that we have a lot of anecdotal data in the humans, but none of the information is measured numbers, and that is where, as a risk assesser, or someone in trying to evaluate the data, it is hard to

make a judgment without having the specific numbers. And, with the animal data it is there, so --

BOARD MEMBER GLANTZ: Well, why don't you -- you were going to go and jump to where you specifically address this point. I think that would be a good idea.

DR. GEORGE ALEXEEFF: Well, I did just want to comment on Dr. Byus' point, and that is that it is correct. I think he is correct in a point, that in this case the assumption is that it is the P-450 and a fellow who is producing these carcinogenic metabolites, so at higher concentrations it would be expected to saturate.

I am not aware of the known concentration that it would saturate for perchloroethylene, but at some point it would, just as it does for all of the solvents. Usually, it is somewhere in the 100 to 500 --

BOARD MEMBER FROINES: But, I feel it is also very important to point out that in the high dose region, you are also likely to have activation by glutathione, which Deccan [sic.] in Germany, has demonstrated and has persistently commented that since P-450 is the overwhelming path, high infinity path for perchloroethylene, that the impact of glutathione mediated by activations not having importance, so that you may have carcinogenicity derived from the glutathione activation that is a high dose intermitter as well.

And one of the problems with not knowing the nature of the human metabolism is that George and co-workers can't deal with the glutathione pathway because they don't know. They don't -- I don't know how much trichloroacetic acid is formed, but that would go -- that would be produced by the glutathione pathway, and so that the uncertainty about the degree of human metabolism really drives this issue and this concern.

And, I do want to make one comment, I think that if you take every compound that this panel has ever gone through, you will find that you don't find the number of cancers in the work place that you would predict in the animal risk assessment data. That is not new. That is something that we've known from benzene to the present. That suggests to me that there may be some basic flaws over all, which is what I hear you saying in the process of risk assessment.

But -- and I am not the person to comment on epidemiology on this panel -- but I do think that that represents a generic problem, not a specific problem as such.

BOARD MEMBER WITSCHI: Well, but what I really meant to say, it is probably going to be a problem of the future, together with mechanisms, together with pharmacokinetics, together with self-proliferation, and

so.

DR. GEORGE ALEXEEFF: Yes.

Although, just to make a comment, there has been a lot of data incorporated into this particular document for metabolism, and then I think that we will see that for formaldehyde we even take it a step further and look at DNA addicts that are formed. And, now there is, as Dr. Froines mentioned, there is likelihood that we are going to try to incorporate self-proliferation in that model.

So, the animal models are trying to proceed as the data becomes available, but that is one of the reasons we state that these are upper bounds, with the idea that as new information comes in, the upper bounds will lower, if assuming we were correct in making our assumptions.

But, getting to the same issue regarding the worker exposure incidences, okay. So, there were two comments made by the Halogenated Solvents Industry.

First is, in the staff response to public comments, staff used a unit risk of 56 x 7-3 parts per million to compute an increase of 20 cancer deaths that would have been projected in the Brown and Kaplan epidemiology study. This computation erroneously assumes that the entire cohort is the relevant sample.

As our earlier comments make clear, however, it is the 615 workers exposed only to perchloroethylene that provide a cause and effect study of exposure.

And our response is, as indicated in Part C a number of epidemiologic studies have been conducted on workers in the dry cleaning industry. As discussed in Section 4 of Part B, under the heading of Epidemiologic Evidence for Carcinogenicity in Humans, these studies generally do not adequately address the concentration and duration of perchloroethylene exposure, or confounding factors such as low socioeconomic status, smoking, alcohol use, and the exposure to other carcinogenic solvents, making it difficult to link human exposure to perchloroethylene with cancer.

In one of the more complete studies, conducted by Brown and Kaplan in 1987, the exposures ranged from 2 to 22 parts per million. Assuming that the 619 workers who were primarily exposed to perchloroethylene were subjected to an average of 12.5 parts per million during working hours over a five-year average employment. A life time average perchloroethylene exposure would be .21 parts per million. And, multiplying the unit risk times the exposure, and the 619 exposed workers, indicates that of a potential increase of seven cancers would be expected of this cohort.

Now, in the study, one of the reasons we didn't specifically mention the 619 is that all of the data for the 619 workers isn't given in the report. But, looking at the three cancer sites that are listed -- first of all, we are only expecting seven to occur out of 619, so the numbers start getting small -- considering the three tumor sites provided in the report, the expected incidence was 16, and the observed incidence was 25.

And, thus even for the perchloroethylene exposed workers, the upper bound incidence due to perchloroethylene exposure of seven additional cancer cases is close to the increase in the observed incidence of nine. So, I assume the other sites, that there was some decrease in cancer incidence. So, probably, it would be less than nine, but the data wasn't provided in the report. But, in comparing seven to nine, we are just saying that there is not, you know, we can't show a difference in that, even if it was seven and three, or seven and four, if it went the other way.

But, at this point, for those three cancer sites that are mentioned in the report, there was an excess of nine, and a predicted excess of seven. And, these increases were not statistically significant.

Now, going further, the other comment from the Halogenated Solvents Industry, on this particular subject

was that using the upper end of the best estimate of the upper bound on the unit risk range presented in the draft Part B report, the predicted risks at or near the old TLV of 200 parts per million are large, and increased cancer incidence would be easily detectable in even general epidemiology studies. Past manufacturing plant experience would indicate that such exposures are consistent with past practices and are likely even to be under estimates.

So, I think this refers to what Dr. Seiber was referring to, that there is some industry data showing high previous past exposures, but the only study that we have that has all of the information together is this Brown and Kaplan study in our report.

And, I just wanted to mention a little bit more about the Brown and Kaplan study, where it states that although the perchloroethylene TLV has decrease from 200 parts per million to 25 parts per million over the past 25 years, according to Brown and Kaplan, "The levels of exposure to perchloroethylene in commercial dry cleaning shops have remained fairly constant since its introduction to the industry."

So, although I can't address the manufacturing sector, at least I guess once they develop the process for dry cleaning it has been relatively constant, the

exposure, as far as we can tell from these investigators, who were NIOSH investigators.

CHAIRMAN PITTS: Could I just ask a question.

When you talk about this drop from 200 to 25, I gather from what you are saying is that that must have been based on noncarcinogenic problems --

DR. GEORGE ALEXEEFF: Right.

CHAIRMAN PITTS: -- rather than carcinogenic.

DR. GEORGE ALEXEEFF: Right.

The TLV, as far as I recall, is not -- I think it is stated in the document -- but it is not based on a carcinogenic inpoint. It is simply based upon preventing noncarcinogenic effects.

BOARD MEMBER FRIEDMAN: Were you going to address the formula that appeared on page 10 of their letter that showed how they calculated the --

DR. GEORGE ALEXEEFF: I wasn't going to address any of that. I use the same -- using the same formula, it simply is -- the question is more like -- more relates to the concentration involved.

The Brown and Kaplan study showed an average of 12.5 as opposed to 200, or the other number. Also the Brown and Kaplan study showed a high turn over in these dry cleaner workers of only five years of employment, and so the estimate of 50 years of working at the job, I

don't know.

BOARD MEMBER FRIEDMAN: So, you agree with the formula, but the assumptions that they use in that little little table at the bottom of the page, are sort of way out of line with the experiences you had?

DR. GEORGE ALEXEEFF: Right, right, well, I agree with, like towards the bottom, of 10 parts per million, and the commenter states that, essentially, all of the other ones there should be some detectable incidence in the population, although they say that probably for that lowest one you wouldn't be able to see anything because of the noise.

BOARD MEMBER FRIEDMAN: And, it is the lowest one that is the most realistic.

DR. GEORGE ALEXEEFF: Well, at least from the data we've been able to obtain.

Okay, now let me go back to the --

BOARD MEMBER FROINES: There is, by the way, a California Occupational Mortality Survey that was conducted a couple of years ago, and it does show increases in cancers in dry cleaner employees, and that particular finding has never been followed up in California, and probably would be worthwhile to look at that.

DR. GEORGE ALEXEEFF: As I mentioned, some of

the studies show some increase in the dry cleaner workers, but I guess the solvents have not been clearly identified.

And, I think a bigger point that was made is the question of low socioeconomic status of the dry cleaner workers and their higher incidence of cancer, so I think, you know, I will be happy to follow up on that.

BOARD MEMBER FRIEDMAN: May I ask a question of Dr. Froines?

CHAIRMAN PITTS: Dr. Friedman has a question of Dr. Froines.

BOARD MEMBER FRIEDMAN: He answered it. I was just asking if that was published, and you said that it was.

Was that one of the studies that was included?

DR. GEORGE ALEXEEFF: No, I think he is referring to an internal report.

BOARD MEMBER FRIEDMAN: It was --

DR. GEORGE ALEXEEFF: An internal state report.

CHAIRMAN PITTS: That is the reference for that, then.

BOARD MEMBER FROINES: It is California --

DR. GEORGE ALEXEEFF: I would be happy to look it up --

BOARD MEMBER FROINES: -- Occupational

Mortality Survey.

BOARD MEMBER FRIEDMAN: But, some of the data, the epidemiological data that was quoted, it doesn't sound very much like we are talking about low-socioeconomic status, when we see excess cancers of the cervix, for example --

BOARD MEMBER FROINES: That is what the California data showed, was all of the excess cancers in women working the that industry. I don't remember the men. It may have been the number of men was too small.

DR. GEORGE ALEXEEFF: Okay, now I would like to discuss the comments from the International Fabricare Institute. It is going to bring us back to some familiar territory we've discussed earlier.

The comment is the technical support document states that EPA classifies perchloroethylene as Group B2 carcinogen. In a January 8, 1991 Federal Register Notice, EPA said that perchloroethylene is hereby deleted from the substances referred to as Group B carcinogens.

So, our response is that the commenter correctly characterizes the current administrative status of perchloroethylene at USEPA. The EPA Human Health Assessment Group, which previously was CAG, or the Carcinogen Assessment Group, concluded in its 1986 addendum that perchloroethylene should be classified

within Group B2.

The Halogenated Solvents Subcommittee of the Science Advisory Board has disagreed, initially concluding that perchloroethylene was best placed in Group C, and subsequently concluding that perchloroethylene could not be made to fit neatly into only one category, and the overall weight of evidence placed perchloroethylene on a continuum between B2 and and C.

More recently, EPA staff has reconfirmed their conclusion that perchloroethylene should be categorized in Group B2 -- that is the staff now.

And, this is in a letter in response to the SAB, perchloroethylene has been listed as a B2 carcinogen in USEPA documents, and this is what lead to a number of the confusions, because the official documents were listing it as B2, when in fact that wasn't apparently the official classification.

And, interim decisions have been made within the agency that are more consistent with a B2 classification, than with the C classification.

So, references, and I guess what I mean in response to that particular is in January of 1991, EPA decided to set maximum contaminant level for perchloroethylene in drinking water. And, I guess the

writers of that report were aware of the controversy between B2 and C, and therefore did not discuss those categories, but used a different categorization system of I, II, and III. Under that system, they placed chemicals in Group A and B in Category I. And, that Category I requires a maximum contaminant level of zero as a goal, to try and reduce it.

And, so what they did in this Federal Register in January is they placed perchloroethylene in Category I, which would be consistent with the B2 classification. Cs usually go in Category II. That is in part what confused us, but, in any case that is just the way that they were dealing with the regulatory environment there, so, in fact it is a C.

Okay, now references in the summary of the draft document will be revised to indicate the history and current status of carcinogenicity evaluated within the USEPA and the Science Advisory Board.

And, a reference on page 1-3 of Part B of the summary will be revised to state, "While EPA staff have recommended classification of perchloroethylene as a B2 carcinogen, such a classification has not been finalized and it remains in Category C. The Halogenated Solvents Subcommittee of the Science Advisory Board recently indicated that perchloroethylene should be placed between

B2 and C classification.

BOARD MEMBER SEIBER: George, you might want to add to that, in your comment about the subcommittee of the Scientific Advisory Board, which you felt -- if I understood it right -- was not leaning towards the B2 classification. Did I understand that right?

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER SEIBER: Because if you say it the way you just said it now, it sounds like the staff at EPA is recommending a B2, but you --

DR. GEORGE ALEXEEFF: Okay.

BOARD MEMBER SEIBER: -- have got to at least counter that with something else, otherwise it is still misleading.

DR. GEORGE ALEXEEFF: Okay, fine, I appreciate that.

BOARD MEMBER WITSCHI: Well, if you look who is on the CAG and who is on the Sullivan subcommittee, and so you regular understand how those different opinions are arrived at. Nothing to do with science. It is political beliefs, or scientific political beliefs, if you know the players.

BOARD MEMBER SEIBER: You are telling me more than I need to know, really.

DR. GEORGE ALEXEEFF: Now I would like to

discuss some more of the comments from the Halogenated Solvents Industry Alliance.

The first comment is that the staff states that -- again -- EPA and perchloroethylene drinking water standards based on the agency's position, excuse me. The staff states that, "The EPA set drinking water standards based on the agency's position that perchloroethylene is a probable B2 carcinogen." This is wrong, and the preamble to the drinking water standards regulation states, "In cases of styrene and tetrachloroethylene, where the agency's cancer classification is unresolved, EPA used its categorization approach to derive a maximum contaminant level goal."

And, our response to that comment is that DHS's staff accepts the correction regarding the administrative status; however, DHS's staff note that while the administrative status of perchloroethylene carcinogenicity is unresolved, the decision to set the EPA maximum contaminant limit goal as zero is consistent with a typical EPA treatment of a B2 carcinogen.

I think I have already mentioned the rest, and it is specifically stated in that report that in setting out that perchloroethylene drinking water standards EPA specifically concluded uncertainties regarding the mouse liver tumors, peroxisome proliferation, mononuclear cell

leukemia, and male rat kidney tumors, were insufficient to discount the sufficient level of animal evidence.

So, it simply again reflects the internal debate going on at EPA.

The next comments is with regard to a published article by Odum, et al. that describes the results of an extensive experimental program to explore species differences in carcinogenicity, and concludes that perchloroethylene is unlikely to cause liver cancer in humans.

The staff response -- this is now what the comment is saying -- the staff response to this comment was to include a paragraph describing it on page 3-2 of the draft Part B report, without in any way addressing its implications for the staff's recommendations, or even recognizing it casts serious doubt on the staff's analysis.

Our response to that is that as indicated in Parts B and C of the draft report, experimental studies have indicated that perchloroethylene is, or its metabolites are, genotoxic and can produce cancers in laboratory animals.

And, then I discuss the genotoxicity data, linogenotoxicity [sic.] data, and when mice were exposed to perchloroethylene by oral or inhalation administration

it produced hepatocellular carcinomas. Exposure of rats produced increased incidence of leukemia and kidney tumors.

The relationship of trichloroacetic acid production from perchloroethylene exposure to tumor production is in part accounted for by using the pharmacokinetic adjustments in the report.

What I mean by that is that the whole pharmacokinetic analysis is assuming that the trichloroacetic acid is probably the major player in the cancer production, and that was also the relationship shown by Odum in the self-proliferation, that it was a trichloroacetic acid.

So, if we model the exposure based upon trichloroacetic acid, you are in part taking that into account; however, in order to indicate that cell proliferation may also play a role in the carcinogenicity of perchloroethylene the following sentence will be added to the summary of the report on page 1-3.

"However, the production of trichloroacetic acid and subsequent peroxisome proliferation may also play an important role in the carcinogenicity of perchloroethylene."

So, our response is to put a statement up front in the summary saying that this is an issue.

The next comment is that the revised draft report reflects a continued unwillingness to make use of the best available experimental information on metabolism, pharmacokinetics, and mechanism of perc, and to make a dose adjustment reflecting the nonlinearity that has been observed in numerous studies.

Our response is that DHS staff believes they have made the best use of the available scientific and medical data in developing the upper bound best estimate of risk, and the evaluation used pharmacokinetics, considered recent uncertainty analyses, and evaluated five different approaches in risk assessment. However, the nonlinearity referred to in the comments is unclear since saturation did not reportedly occur in the chronic bioassays, unlike that observed from methylene chloride.

The next comment is a little more specific, and it says that page 5-8 of the draft report states that 82.3 percent of an oral dose of 500 mg per kg was metabolized after administration to mice. And, as authority to this the report cites the work of Schumann. This is incorrect. In the work cited, Schumann clearly states that only 17 percent of the material was metabolized.

And, it further states that page 5-8 of the draft report states that 80 percent of perc inhaled

during radiochemical inhalation experiment in mice was metabolized. This is also incorrect. The actual value is 88 percent. And, it further states that the use of either number in this way is incorrect. The number reported in Schumann et al. is a percentage of the radioactivity recovered after the conclusion of the initial inhalation exposure. And, the minute volume of mice can be estimated from Anderson et al.

And, it goes on to say that using the percentage of inhaled perchloroethylene you can more accurately determine that 49 percent metabolism occurred in the species instead of 88 percent.

Now, the reason why I put all of those comments together is that this is misinterpreting that section of the document. The document is actually discussing a comparison of total metabolites versus urinary metabolites, because all of the estimates of the human data and the animal data are based on urinary metabolites that were measured. So, if you only have urinary metabolites you have to get some estimate of what is the total metabolism. The numbers that were stated in that section are correct.

What it goes on further to say on that page is that while the mice seem to have 80 to 88 percent of their metabolites as urinary metabolites, rats only have

58 percent of their metabolites as urinary metabolites.

So, then the question is then, well, what is the story with humans? We don't know what the answer is, but all that we have measured is 4 percent of urinary metabolites. So, the question is, well, how much of the metabolites could there be? So, that was the purpose of that paragraph. It wasn't trying to discuss what was implied by the comment.

The next comment is that the author's conclusions that the percentage of inhaled perchloroethylene which undergoes metabolism will continue to increase towards 100 percent, as concentrations well below the Km is inconsistent with known principles of pharmacokinetics.

The document states that there is an increase in metabolism when the concentration decreases. The document further states, you know, that under theoretical conditions you might assume it goes to 100 percent for rodents, but we will just -- we were going to eliminate that statement that it might go to 100 percent, in response to this comment, and just simply state that as you would go to lower concentrations, you would expect more to be metabolized, since it was just a --

BOARD MEMBER BYUS: Would be a greater percentage, not the total amount?

DR. GEORGE ALEXEEFF: -- percentage.

BOARD MEMBER BYUS: Right?

DR. GEORGE ALEXEEFF: Right, greater percentage metabolized.

So, we will make that correction there.

But, it does, I think, clearly state in the document that the upper physiological limit in humans is 73 percent and not 100 percent, and also that the risk estimate that we based our analysis on is on a 25 percent human metabolism and not 100 percent human metabolism rate.

BOARD MEMBER BECKER: Check to see whether trichloroacetic acid, you can account for 25 percent metabolic scheme to trichloroacetic acid, when there has been programmed exposures to perchloroethylene?

In other words, you just assume for each of the models --

DR. GEORGE ALEXEEFF: No, there are a number of studies that looked at urinary metabolites.

Now, the purpose of most of the studies were not to do what we are trying to do here. Just like, as the animal studies for cancer were not based for risk assessment per se.

The human studies were to try and find a urinary metabolite to tract exposure, so they could get

estimates on how much workers were being exposed. So, they are simply trying to find a good surrogate, so they weren't trying to account for everything. But, they did find trichloroacetic acid compounds, and there are several studies, mostly Japanese, but also some other studies, showing that for the trichloro compounds, the range is in the 2 to 4 percent. I think that is pretty well defined for those compounds. In humans it is 2 to 4 percent.

BOARD MEMBER BECKER: That is the major reason that you differed with EPA, right? Because they just assumed 4 percent.

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER BECKER: And, then you used the 25 percent?

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER BECKER: And, then that leads to the eight-fold difference?

DR. GEORGE ALEXEEFF: Right.

Okay, and the last comments we have already discussed. Those were the ones dealing with Brown and Kaplan's report.

BOARD MEMBER FROINES: It is worth mentioning about what Dr. Becker has said about that.

I think what had us upset about that, I mean,

that he has, you know, there are people who have suggested that there are higher levels of metabolism.

DR. GEORGE ALEXEEFF: Yes.

And, just in response to that, that is one of the reasons that we came up the 25 percent, was through Dr. Hattis' suggestion. There were several studies by different investigators. One is the Bois, et al. study in 1990, and they did a Monte Carlo simulation of all of the uncertainties, and came up with a -- I mentioned in the report -- they came up with a risk number very close to ours. I think in theirs it is 7, instead of in ours it is 8 x 10 -6, using this Monte Carlo simulation for uncertainty.

Bogen and McKone were the investigators who came up with a roughly 73 percent physiological limit for humans, of metabolism. And, then Dr. Hattis has his own model and came up with an estimate which he felt was a reasonable upper bound of 25 percent. So, it is on those numbers, which the EPA didn't have in their 86 assessment, that we came up with a different decision from EPA.

And, the reason we had rejected pharmacokinetic analysis in the original draft that we sent out for public comment, was specifically the human metabolism data, because it didn't seem to us scientifically valid

to say, well, we haven't found 20 to 60 percent of the human dose, but we are just going to assume that it was just four percent. So, we felt that until some handle was given, as to what else might be metabolized, and other investigators, obviously, had similar concerns, and they generated what might be these upper bounds if we made different physiological assumptions, used different models, and they came up with that range, and we felt that 25 percent was a valid upper bound, and we are willing to accept other comments if you feel another upper bound is more appropriate.

Anyway, that is the end of my presentation.

BOARD MEMBER SEIBER: George, I have a question we haven't really dealt with exactly here, but it is seems like for trichloroethylene you'd had an excess cancer prediction of one number. It was like two or three per million, or something like that. For perchloroethylene it is more like 50. What is the biggest difference in the data set which makes one so much higher than the other one, when they are fairly similar compounds? Am I quoting that right?

DR. GEORGE ALEXEEFF: Let's see.

BOARD MEMBER SEIBER: It seems like we have to rely on some analogy with trichloroethylene, which has already gone through the process here, hasn't it? With

an even lesser excess cancer -- that is the bottom line prediction.

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER SEIBER: What really explains the difference between the two, and is there so much uncertainty that you really can't differentiate between the two compounds? It is a tough question.

DONALD AMES: I am trying to recall -- I guess you would be right. It would be 54 -- oh, you have the numbers here?

[Pause in the proceedings.]

DR. GEORGE ALEXEEFF: Okay, yes,

BOARD MEMBER SEIBER: In the findings, is that right?

DR. GEORGE ALEXEEFF: -- yes.

If you look at per micrograms per cubic meter, the difference is really only four-fold, as opposed to 50. Maybe you were thinking of the micrograms per cubic meter for trichloroethylene, and the ppb for the other. That would multiply it by 7.

So, it is 2 x 10 -6 for trichloroethylene, and 8 x 10 -6 for perchloroethylene. And, I would say that that is within a lot of the uncertainty. Probably the difference is mostly due to, I think, a slightly lower dose in the perchloroethylene study. I think it was 100

and 200 parts per million, and I think it was 200 and 400 in the trichloroethylene studies. So, I think that accounts for some of the uncertainty involved there.

But, from those who are involved in risk assessment, the number of assumptions, I think we have laid out a lot of the uncertainties. I think it would be hard for us to argue that 8 is significantly higher than 2. Usually, we go 3-fold as being a reasonable area but then --

BOARD MEMBER WITSCHI: Excuse my ignorance, but what is worse? Or, what is the bigger risk? The bigger number?

DR. GEORGE ALEXEEFF: The bigger number is a worse risk --

BOARD MEMBER WITSCHI: The bigger risk.

DR. GEORGE ALEXEEFF: -- and has a higher potency. It is just how the data fall out.

BOARD MEMBER FROINES: People who deal with science, real science, don't like differences of 3 or 4. People who deal with risk assessment take 3 to 4 orders of magnitude as being some sort of experimental error, so then that is --

DR. GEORGE ALEXEEFF: Yes, not order of -- yes, 3-fold or 4-fold in this case, but not order of magnitude.

BOARD MEMBER GLANTZ: Well, George, one thing, I mean, when I was getting ready for the meeting, I read through -- as I usually do -- Part C first, and you know there was a lot of complaining in there about not using a pharmacokinetic based model. Then, when I went and read Part B, I thought, well, gee, it looked like the whole thing was based on a pharmacokinetic based model, so just for my -- so, I am sure that I am not hallucinating -- basically, what happened was that originally you didn't use the pharmacokinetic model, and then in response to a combination of the public comments, plus the availability of new data, it sounds like you've completely changed it around, and used exactly the approach --

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER GLANTZ: -- that was being advocated in the --

DR. GEORGE ALEXEEFF: Right, and we threw out the applied dose data. We don't even include it in the range even.

BOARD MEMBER GLANTZ: Okay.

BOARD MEMBER SEIBER: So, I guess, getting back to my earlier comment, and it seems like -- and this was before I had joined the panel, I believe -- that an action was taken on trichloroethylene with an estimated life time excess that was even lower than the one that we

are considering here. I just wanted to make sure that I understood that properly.

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER SEIBER: And, it was only 2 or 3 per million is the actual number.

DR. GEORGE ALEXEEFF: You know, I think you probably include in your calculations the exposure in the environment. That must be what it is.

BOARD MEMBER BYUS: Yes, with trichloroethlyene, I believe that it was just that there -- the reason it was -- we considered almost not declaring it a toxic air contaminant. We did discuss that, and again it was based on what the lead considered moderate animal data, weak animal data, no human data, that I recall.

I'm trying to think. The other differences might be that the tumors in the animals were not liver tumors, they were other sites than the liver indicated.

The reason we didn't have this discussion at the time was that the exposure levels were so low in the state that it only accounted for several excess cancers per million, and we actually recommended to the Board that they -- we actually made a statement in there, to the effect that this probably was an upper limit, and this was not -- we didn't feel that this was a major

concern, at least nonoccupational, so there really is the difference.

And, there was virtually no public comment, because, I think it wasn't --

[General discussion.]

-- it was even used that much, although I can't really --

[General discussion.]

-- so, all in all, we never really --

BOARD MEMBER FROINES: But, if you want to take it to the next step, I don't remember the numbers, either, but the cancers that were found from ethylene chloride were at 2000 and 4000 parts per million, so its risk is significantly lower than what we are talking about here, by an order of magnitude, I think.

Is that right, George?

DR. GEORGE ALEXEEFF: It is not an order of magnitude. It is 1 x 10 -6, so it is two-fold below trichloroacetic acid, so actually it is eight-fold below the perchloroethylene number, you are right. So, it is roughly an order of magnitude --

BOARD MEMBER FROINES: In terms on tonnage, hydrocarbons was the compound that demonstrated the least risk, and then you have trichloroethylene, which is almost identical to perchloroethylene, so that -- and so

you could almost do a back-of-the-envelope calculation of what the applied doses were in the bioassays to come up with those numbers.

BOARD MEMBER BECKER: More was known about the metabolism of methylene chloride, so that the scale with the different metabolic schemes and its saturations kind of made it easier, and I think, in general, when you can learn more about the metabolism, the numbers have fallen, and demonstrated that here also when you applied the modeling, the numbers fell further.

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER WITSCHI: I was wondering, George, how comfortable you feel with the qualitative aspects of the evidence for carcinogenicity? And, there are two reasons. The one is, first of all, the only good tumor data there really are, with the chlorosadene [sic.], are the liver tumors in the B6C3F1 mice, and they are notorious for being attacked as not being -- a kind of fluke of nature.

The other, which is also, it is kind of a problem is the punitive mechanism of perchloroethylene carcinogenicity, which from the evidence we have it is a peroxisome proliferator and from what people think about peroxisome proliferator they definitely, or more or less definitely, you would have a threshold for their

activity.

And, in your point two, you know, on the summary of the finding, it comes again this standard preamble that no evidence of a level below which no carcinogenic effects are anticipated. And, I think, in in view of, at least some people belief in the peroxisome proliferation and threshold theory this needs to be given some thought.

What I am really wondering is, and I am not going to second guess IARC, not after what I said -- you know, but there is some with this particular compound, it is not that easy to decide whether it is an animal carcinogen or not, or what that means, the animal carcinogenicity data.

DR. GEORGE ALEXEEFF: Well, I can say that I feel as comfortable with this compound as a number of the other ones that have been brought to the Board, particularly a number of the other solvents, trichloroacetic acid, methylene chloride, and carbon tetrachloride.

I think, overall, that they have a number of the same concerns that you just raised, and it in part has to do with the nature of the data. And, also, I think there is the other fundamental issues that you raised with regard to self proliferation, let's say for

example, so then --

BOARD MEMBER WITSCHI: No, no, no, so let's get this straight, and that is the pathologist in me.

Peroxisome proliferation is not self proliferation, these are two different things.

DR. GEORGE ALEXEEFF: Okay, peroxisome proliferation.

In any case, the methodology for incorporating that kind of information is trying to be developed by staffs of EPA and our Health Department staff, but it is not something that we have been able to come to any conclusion about, as a department. And, so I am not sure if in the guidelines that come out in a year or so if we will have a better handle on it, but I think that is a fundamental question.

BOARD MEMBER WITSCHI: Yes, no, I wouldn't have expected you to have an answer, but I think this is something, if you look into the future, that really -- and I am glad that you are aware of those things, and you've considered them.

DR. GEORGE ALEXEEFF: Right.

BOARD MEMBER WITSCHI: It will come.

DR. GEORGE ALEXEEFF: Right.

Now, something that has come back to my mind is just a comment you had made earlier, and I just want to

mention that for let's say cadmium, which is a different kind of chemical, a metal, in that, when we brought that to the Board, we decided to -- again do something different from EPA -- we chose to base the risk on the human study that had just come out, and it showed a risk at least ten-fold lower -- I can't recall precisely -- but at least ten-fold lower than the animal data, and that is what we had proposed to the panel, and the panel had accepted. Then, subsequently, EPA also revised its estimate, as well.

So, in that analysis we went through the human data very carefully and tried to say, is there something in this human data which tells us that we shouldn't use it, or can we feel confident that this human data, you know, is a valid upper bound, because, again, we are talking upper bounds in our case, and we decided that it was, based upon an analysis of the data.

So, we try to -- if we see the data can withstand that kind of analysis, we try to do that kind of thing and use human data where possible, even though for like cadmium, the data for human carcinogenicity is limited, yet we still use the human number for that, instead of the animal number, because we just felt that it would be a more valid number.

So, if human data were better available for

some of these halogenated solvents, although there are some good studies, particularly with methylene chloride, but, when you analyze them the power of the study, and the uncertainty in the study is so large that it overlaps with the animal information, and so it doesn't really tell you a lot.

BOARD MEMBER FROINES: Just following up on his comment, and maybe you can comment, the other question that occurred to me is this is a fairly cytotoxic material, with respect to the liver, at the doses that may have been used in the chronic animal bioassay, and so if you hypothesize -- hypothesizing meaning metabolically formed -- and then the innate addict formation having occurred, and then since those cells aren't turning over, they are just sitting there, you don't get, without the cellular proliferation, you wouldn't get initiation, and that the cytotoxicity of the perchloroethylene may have something to do with fixing the genetic event.

And, so one could also conceive of a threshold using cytotoxicity and not peroxisome, as well.

BOARD MEMBER WITSCHI: Yes, and I would agree with that one.

BOARD MEMBER FROINES: I don't know, I mean, I don't know whether -- I don't think there is any data to incorporate like there is with formaldehyde, that sort of

thing into this kind of process, so I would suggest it, but it does seem to me that that is also a possibility.

We certainly have seen that with the differences in carcinogenicity between a 2-4 and 2-6 dynam taruene [sic.]. The only one that is carcinogenic is the one that kills liver cells, causes cytotoxics, and so it seems to me that that is another possibility that could be occurring in this case. I don't think you can incorporate, but I think it is worth thinking about.

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER DAVIS: I would like to make a comment about the epidemiology part of the thing, not being an epidemiologist myself, but fundamentally somebody with a background in clinical trials, where most clinical trials prospective randomized are negative, they are not always negative because they are negative. They are usually negative because the sample size was wrong, so you get 100 in RMA and 100 in RMB and there is no difference, and that does not prove that there is no difference. If you set up to your trial in advance to know what difference you are looking for, you may have to enter a 1000 patients in a lin in order to be able to see the difference, with a kind of P value and power that you are interested in.

And, one of the problems here is on this page

10 that we have he made this astonishing calculation where he gets 79 percent cancer out of the situation with your risk estimate, and that 79 percent, that has to sit on top of the 25 percent risk we are all at in this room, and that makes 104 percent likelihood that any worker at 200 units for 30 years is going to get cancer. That is a little more than unity.

And, then he gets a little more sober as he goes down on the table, and gives lesser parts per million, and lesser number of years.

And, I guess what I would like to see at some juncture is that we say not that there is no evidence in the literature, epidemiologically, to support this kind of risk, but to model it, if you will, and at what sample size would we have to do the study? For five years and the expected 25 parts per million, so that we can, I think, with in the context of our document, discredit these kinds of Philistine attacks that say. look, you don't have a study to prove that this causes cancer in humans, therefore it all wet. I don't think that that is true at all. I think that you can handle that in a more sophisticated way, like I suggest.

And, again, possibly, the real epidemiologist on the panel could help you with that, because my experience is actually estimating differences in

prospective trials.

But, I don't like the business of no study confirms, because that is just not true. No study was of the sample size to be able to confirm, in truth. I think that is the problem here.

BOARD MEMBER GLANTZ: Yeah, and you know, I think that is a very good point, and I think, as a -- you know, as we sort of go on we add things, kind of put in these reports routinely, and I think that kind of a power analysis of the available epidemiology is a very, very good idea, and it is not all that hard to do, actually.

But, it really does create a much better context in which to look at these things, because if you come up with a negative study that has an 85 percent power, it could be a lot more confident than a negative study with a 4 percent power. And, most of these studies are closer to 4 percent than they are to 85 percent, just because of the problems of accumulation, and not because anybody is being naughty. It is just hard to get enough patients.

BOARD MEMBER DAVIS: But, he is getting us closer in that table to figure out how many cancers we are really looking for. It is six at the bottom with 25 parts per million for ten years. I think, if you do the arithmetic, 25 parts per million for five years, it

probably goes down to three, and so what kind of study do you have to do to find three extras?

BOARD MEMBER GLANTZ: That's right.

BOARD MEMBER DAVIS: And, I think those studies are undoable, quite frankly, and maybe I might get disagreement from my right, but I doubt it.

BOARD MEMBER GLANTZ: But, I think that is a very good thing to -- I mean, I don't know if you necessarily need to do it here, although it wouldn't hurt, but I think in the future that would be a good thing to just add, is just a little power table.

I know that I can't go to a meeting without mentioning ETS. I mean, we ended up doing that in our heart disease study, and looking at the different things that were out there on ETS and heart disease, and it really was very sobering when you see these studies with three and four and five percent power. It kind of puts a different cast on the fact that it wasn't statistically significant.

So, I think we ought to just routinely do that.

DR. GEORGE ALEXEEFF: I see.

CHAIRMAN PITTS: Now, we have, I notice, some sort of a lull here in our discussion. We can handle that lull by lunch. And, perhaps fortified by having lunch, it might be useful then to return --

Yes, Gary.

BOARD MEMBER FRIEDMAN: Some of us have to catch a 2:00 o'clock plane, so I was wondering if we could come to closure.

CHAIRMAN PITTS: Oh, well, it is diet time, then.

BOARD MEMBER GLANTZ: Well, you can always reschedule flights, that is not hard.

I guess, how long is the formaldehyde discussion going to take? Because I don't think we can finish this, and talk about formaldehyde at any length and catch a 2:00 o'clock flight.

BOARD MEMBER FROINES: We don't need to have that discussion with the panel.

BOARD MEMBER GLANTZ: Okay.

BOARD MEMBER FROINES: It is a question of, if we incorporate self proliferation, how long is that going to take DHS? And, then when will it come up?

CHAIRMAN PITTS: Well, I am more than happy, if you feel that we want to, let's continue the discussion. I wasn't aware that it was a 2:00 o'clock flight.

All right, then let's --

[General discussion.]

Well, that kind of takes care of things, too.

Why don't we start then, open it up for

discussion, formal discussion, and we'll start right over here and work our way around the table.

Any comments?

BOARD MEMBER WITSCHI: No.

CHAIRMAN PITTS: Tom?

BOARD MEMBER DAVIS: No extra comments.

CHAIRMAN PITTS: No additional comments? All right.

BOARD MEMBER FRIEDMAN: I'm not sure what you are asking for.

CHAIRMAN PITTS: I am asking for comments on the overall document, comments on the discussion today, comments prior to a motion. We may have comments after the motions. I would like to hear what the motion is going to be. But, just sort of a quick run through to see where we are.

If you wanted to go back with further discussions?

BOARD MEMBER FRIEDMAN: No, not now.

CHAIRMAN PITTS: How about you, Craig or Stan?

BOARD MEMBER BYUS: No, but I just wanted to say that I thought the pharmacokinetic analysis was very good, and glad to see it was such an extensive analysis in this document, even though it is far from a clear

story, it is very good.

CHAIRMAN PITTS: Any others?

BOARD MEMBER BECKER: I think that I do have one comment, just in passing, and that is it is very -- and maybe I am the only one -- but I have learned an awful lot today from the meeting, that this was really one of the best meetings I've attended. I had read the information, but the responses as they came back confused me some, and I think we learned a good deal about how this group operates in a more efficient manner, and I found this meeting very productive in the learning process, and how to deal with this.

And, I think the answers provided to Part A and Part B were superb, and I believe it really helped to address them honestly and openly, because we discussed it on the airplane and we were confused, and I have been satisfied.

CHAIRMAN PITTS: Stan.

BOARD MEMBER GLANTZ: Yeah, me too. I would like to second what Chuck said. I feel very much the same --

CHAIRMAN PITTS: Can't hear you.

BOARD MEMBER GLANTZ: -- I feel very much the same way Chuck did. I was very concerned. I mean, I was very, very concerned about this report when I read the

Part C and the other letters before I heard what you had to say here, and I am satisfied now.

CHAIRMAN PITTS: Now, we have a preliminary draft, sort of a revised, revised sort of a draft, of possible findings from this panel, and so I would think that we would want to examine those --

BOARD MEMBER FROINES: Can I ask George one question.

CHAIRMAN PITTS: Shoot, sure.

BOARD MEMBER FROINES: Because this goes to what we did with methylene chloride, and I would like to put it to rest before the panel instead of -- do you think that -- you used the Hattis upper bound percent metabolism for your estimating dose, ultimately, in the model, and so you are using some level somewhat, but as one would consider is an upward bound, and my question is do you still need to incorporate the surface area correction, given that that is another level of conservatism?

In methylene chloride, the document has one of the values, the risk number without the surface area correction, and so what I guess I am asking you is do you feel that you need to keep that surface area correction in for reasons that you have got evaluation of uncertainty, you have got upward bound on metabolism,

you've got a lot of conservatisms built in, and so if you need the surface area correction, I think you should be able to say, yes or no.

DR. GEORGE ALEXEEFF: Well, the answer is, yes, and it was stated in the document as to why we felt we need to retain that.

The 25 percent for the metabolism simply refers to the pharmacokinetic data portion of it, and not either the pharmacodynamic aspect of it -- or actually for the perchloroethylene there is a lot of data showing human variability. As well, in response, there were, you know, some studies on working and non-working in diet, and that sort of thing, so we felt that the surface area correction served a different function than the upper bound metabolism corrections, so that was our staff opinion.

BOARD MEMBER FROINES: Let me just say why I raised it, for members of the panel.

When I present this to the Board in October, whenever this issue is going to come up, I just want to make sure we are on record as to how we are addressing it, and I am happy with what you did.

I think one could make an argument to put it in, but I think -- I recommend leaving it, but it will come up again, because we are not going to be free of it.

BOARD MEMBER BYUS: Is the surface area correction, is it -- it is clearly done for pharmacodynamic reasons, in terms of dose?

DR. GEORGE ALEXEEFF: Yes.

BOARD MEMBER FROINES: It is part of his pharmacodynamic safety factor.

BOARD MEMBER BYUS: Right.

BOARD MEMBER FROINES: That is what he is saying.

BOARD MEMBER BYUS: Is it?

DR. GEORGE ALEXEEFF: Yes.

CHAIRMAN PITTS: Now, we have this preliminary revised preliminary draft here of the findings. I would request each member of the panel to go through this, if you haven't already, and then we'll open this up for discussion, because the motion will then be based upon the considerations of this document.

BOARD MEMBER BECKER: There is the major change from what we were given in the draft, that is number 1, is that correct?

CHAIRMAN PITTS: This certainly is a major change.

Who would like to address that from the ARB?

The first thing that I think we should, as a group, agree that what changes that we may make in -- may

have been made in these findings should be reflected in the executive summary and then in the body of the document, for the record. I presume that it will, but for the record we want to be sure that those changes are reflected so there is a consistency between the two.

And, Joan, I am sure you will do this, right?

DR. JOAN DENTON: Will do.

CHAIRMAN PITTS: Okay, fine.

Let's see, who would like to comment on these.

Stan, let's start with you first.

BOARD MEMBER GLANTZ: I think that -- I read this over and it looks fine to me.

[MOTION]

I'll move that we adopt it.

CHAIRMAN PITTS: All right, is there a "second" to the motion?

BOARD MEMBER BECKER: Second.

CHAIRMAN PITTS: Dr. Becker, so it is moved and seconded that we adopt the findings.

It is open for discussion.

BOARD MEMBER FRIEDMAN: I have just a couple of things.

CHAIRMAN PITTS: Yes, sir, Dr. Friedman.

BOARD MEMBER FRIEDMAN: Point number 1, I wonder if in the third to the last line you should say

the panel concurs with the EPA staff, because of the EPA's official, as has been discussed here today, their recommendation is different.

BOARD MEMBER SEIBER: Well, that raises a question. Were the comments we had earlier this morning, are they in here? Or, is this something that they just whipped out? Or, is this -- you've got --

CHAIRMAN PITTS: Bruce, do you want to address the history of this?

BRUCE OULREY: Yes, if you'd like, I can go ahead and cover the changes that we included.

The first one here, earlier it said the United States Environmental Protection Agency recommended perchloroethylene be assigned to Group B2, of its classification scheme for carcinogens. And, then we go on there.

What we changed there is we said staff of the United States Environmental Protection Agency

Okay, and then --

CHAIRMAN PITTS: Dr. Friedman's comment would clarify that by adding --

BRUCE OULREY: Right.

CHAIRMAN PITTS: -- in the last few lines, based on available, the panel concurs with the EPA --

BRUCE OULREY: Staff.

CHAIRMAN PITTS: -- we would insert staff.

BRUCE OULREY: Right.

BOARD MEMBER FROINES: But, wait, I was going to ask the same question, because the word potentially is not possibly or probably, and that is the issue. It is really not -- the word potentially in a sense obfuscate the issue, because the issue is B2 says probably, and C2 says possibly.

So, you use the potentially, and therefore, does potentially mean possibly? Or, does it mean probably? Or, does it cover the whole range.

BOARD MEMBER GLANTZ: I think that we should say probably.

BOARD MEMBER FRIEDMAN: Well, doesn't the IARC say possibly?

BOARD MEMBER FROINES: Yes.

BOARD MEMBER FRIEDMAN: I would vote in favor of possibly.

BOARD MEMBER GLANTZ: Okay.

BOARD MEMBER FROINES: Nobody says anything but possibly.

CHAIRMAN PITTS: That's correct, and --

BOARD MEMBER GLANTZ: Okay, then I would think --

CHAIRMAN PITTS: -- and I think we should --

[General discussion.]

BOARD MEMBER GLANTZ: -- we should say possibly.

BOARD MEMBER FROINES: Except for the staff, the EPA staff.

BOARD MEMBER DAVIS: Here it says in this document, if you read just the second sentence of 1, the international agency, IARC, list perchloroethylene in Group 2B. That is there possibly, is it.

BRUCE OULREY: That is possible, correct.

CHAIRMAN PITTS: That is possibly, based on animal studies, and not human epidemiology, that is correct.

[General Discussion.]

BRUCE OULREY: Dr. Froines, are you recommending then, on the very last sentence of the first finding, that it be probably carcinogenic?

CHAIRMAN PITTS: Possibly, no, no.

BOARD MEMBER FROINES: I am not recommending anything.

All that I am saying is if we say the panel concurs with -- I don't understand why you have all of the V's in there by the way, but that is beside the point -- the panel concurs with EPA, IARC, and DHS, that perchloroethylene is carcinogenic for animals, and

possibly carcinogenic for humans.

If you want to say probably, then you have to say -- you have to break that sentence up --

CHAIRMAN PITTS: No, no, no, you can't because IARC doesn't --

BOARD MEMBER GLANTZ: We want to use the same word.

BOARD MEMBER FROINES: Yes.

BOARD MEMBER FRIEDMAN: We agree with what Dr. Froines said, potentially is very vague --

BRUCE OULREY: So, we will change it to possibly.

CHAIRMAN PITTS: Yes, and that is consistent with the IARC classification, and I think probably with their thinking, too, isn't that more importantly than it is possibly, but it is not --

BOARD MEMBER FRIEDMAN: I have another question. I am sorry I didn't ask about in the presentation of Part A --

CHAIRMAN PITTS: No, no, that is all right.

BOARD MEMBER FRIEDMAN: -- but in number 6, when it talks about the life time as approximately 150 days, is that a half life? In other words, does a molecule of perchloroethylene sit there, and then suddenly in 150 days gets destroyed, or?

BARBARA COOK: That is atmospheric life time, it is not a half life.

BOARD MEMBER FRIEDMAN: What is that --

CHAIRMAN PITTS: It means the time, if you have a thousand of them, in that length of time it will drop to 1 over E, the base of natural logs, and which is almost a half life.

BOARD MEMBER FRIEDMAN: Does that mean they will all go?

CHAIRMAN PITTS: No, half of them will disappear, and then another --

BOARD MEMBER GLANTZ: But, no, 1 over E isn't

[General discussion.]

BARBARA COOK: It is about 37 percent.

CHAIRMAN PITTS: Well, just roughly, I mean, you can assume that it is a half life.

BARBARA COOK: It is about 37 percent.

BOARD MEMBER FRIEDMAN: But, I mean, that --

CHAIRMAN PITTS: Okay, 37 percent.

BOARD MEMBER FRIEDMAN: -- life time is sort of a technical term that you guys know what that means, I just --

CHAIRMAN PITTS: Okay, well, let me say it again, what it means, if you have -- let's use it in terms of a half life first.

If you have a thousand, and when you say, because often it will say T 1/2 -- half life -- 500 will be around at that number of days, there will be 500. Then 100 and some-odd days later, there will be 250.

BOARD MEMBER FRIEDMAN: So, in other words, it is a tropospheric life time is a half life, is that what that is?

CHAIRMAN PITTS: It is close.

A tropospheric life time is actually 1 over E, 1 over 2. -- what is it --

BOARD MEMBER FRIEDMAN: I mean, just as long as we know --

[General Discussion]

CHAIRMAN PITTS: -- oh, yes, that is how we define them.

BOARD MEMBER GLANTZ: When you say life time, do you mean time constant, for those of us who --

CHAIRMAN PITTS: It is not a rate constant, it is a time for it to drop to 1 over E, the number one over the letter E --

BOARD MEMBER GLANTZ: Right, but that is called the time constant --

CHAIRMAN PITTS: Well, and an atmospheric chemist calls it an atmospheric life time. It is referred --

BOARD MEMBER GLANTZ: Oh, okay.

CHAIRMAN PITTS: -- as the first order of decay for --

BOARD MEMBER GLANTZ: Oh, okay.

CHAIRMAN PITTS: -- and you make an assumption of a hydroxal radical --

BOARD MEMBER GLANTZ: Okay, okay, so --

BOARD MEMBER FRIEDMAN: For those of us, and probably other members of the Board who don't understand, I think it should be defined in clean English --

CHAIRMAN PITTS: Exactly, and that is why we use to fight to have the definitions in the document, itself.

They are still there, aren't they?

JOAN DENTON: Yes, they are.

CHAIRMAN PITTS: But, they are not in here. And, actually, I am always happier, because when you try to explain 1 over E, you get involved. It is close enough to half life, then you can figure out it goes to half the value, like the nuclear disintegration has a half life of so many years. Half the nuclei go in that period, and then the rest of them go in the other half.

What? I like half life better myself, because it makes -- why do you have to go to 1 over E which you can derive from something? I think in the future half

life. I think that is a much more --

BOARD MEMBER GLANTZ: He can just afix the number.

BOARD MEMBER BECKER: -- then you can just say -- and it is usually written as T 1/2 then, which defines it as --

BOARD MEMBER GLANTZ: It is times the log of --

CHAIRMAN PITTS: -- a given power --

BOARD MEMBER GLANTZ: -- divided by the log --

CHAIRMAN PITTS: -- which is a --

[General discussion.]

All right, good point.

Next.

BOARD MEMBER DAVIS: If we make that change, then is it true T 1/2 is 1/5?

BOARD MEMBER GLANTZ: No, it will be a different number.

CHAIRMAN PITTS: It will be a little different.

BOARD MEMBER GLANTZ: It will be this divided by the log of 2, I think --

CHAIRMAN PITTS: Yes, that's right.

BOARD MEMBER GLANTZ: The natural log of 2.

CHAIRMAN PITTS: That's right, it is about .37, or something.

BRUCE OULREY: Okay, we can fill in that

number.

CHAIRMAN PITTS: Why don't we do that. I think that ought to be getter in the future, too, because it is always such and such.

BRUCE OULREY: Okay.

CHAIRMAN PITTS: It also, what it basically means is it hangs around for a long time and gets distributed over a long base.

Okay.

BRUCE OULREY: The other change that was made in the revised findings is that in Finding No. 4, I believe it is the sixth line down, after the bracket. It says:

> "This level is 8-fold greater than the level in the 1986 draft EPA health assessment, due to DHS incorporation of recent data accounting for uncertainty on human metabolism.

So, that has been added to the findings, as a further refinement.

CHAIRMAN PITTS: I don't think I had -- my concern about that sentence there is I don't understand it. It says -- I mean, there are more uncertainties in me than in that -- it is more than 8-fold.

BOARD MEMBER GLANTZ: Well, why don't you just delete the accounting for uncertainty, and just us

incorporation of recent data on human metabolism.

BRUCE OULREY: Okay, so incorporation of --

CHAIRMAN PITTS: I would appreciate that --

BRUCE OULREY: -- okay.

CHAIRMAN PITTS: -- remove my uncertainty.

BRUCE OULREY: We will just get rid of all of the uncertainty here.

Okay, that's been noted.

BOARD MEMBER GLANTZ: But, that isn't accurate, either, though.

CHAIRMAN PITTS: What's that?

BOARD MEMBER GLANTZ: Accuracy.

[General discussion.]

BOARD MEMBER BYUS: Why do we need to say that at all?

BRUCE OULREY: Pardon me?

CHAIRMAN PITTS: All right, and any other comments on the findings?

BOARD MEMBER BYUS: Well, let's not leave that, though.

So, what is that going to be now? You were going to include this because of the comments that were received?

BRUCE OULREY: Okay, would you like me to re-read that?

BOARD MEMBER BYUS: Yes, and what is it going to say?

BRUCE OULREY: This level is 8-fold greater than the level in the 1986 draft EPA health assessment due to DHS incorporation of recent data --

BOARD MEMBER GLANTZ: Period.

BRUCE OULREY: -- on human metabolism.

BOARD MEMBER GLANTZ: Just period.

BRUCE OULREY: Okay, so you don't want to include the human metabolism?

BOARD MEMBER GLANTZ: Well, John says it is not quite correct to say that.

BOARD MEMBER BYUS: It is not really data. It is more assumptions.

How would you interpret that? Is it data?

CHAIRMAN PITTS: Do you want to say information, instead of data?

BOARD MEMBER BYUS: It is there for this is using the 25 percent.

CHAIRMAN PITTS: It is information, maybe, rather than data.

BOARD MEMBER FROINES: George.

DR. GEORGE ALEXEEFF: I don't know what you are talking about.

[Pause in the proceedings.]

I think it is either information or analysis.

BOARD MEMBER BYUS: Analysis is a better word.

[General discussion.]

DR. GEORGE ALEXEEFF: It is a Monte Carlo simulation, and I wouldn't call it data. I'd call it that someone just analyzed the existing data.

BOARD MEMBER BYUS: So, what word are we going to pick? Analysis?

CHAIRMAN PITTS: Analysis? Is that singular or plural? It is plural, analyses, isn't it?

BOARD MEMBER DAVIS: I think, grammatically, it may become "of" rather than analysis "on".

[Pause in the proceedings.]

BRUCE OULREY: Of, okay.

BOARD MEMBER BYUS: Analysis of human metabolism? You want to leave the human metabolism in or, not?

BRUCE OULREY: Is that correct to say that?

BOARD MEMBER FROINES: Read it again to me. I've lost it.

BRUCE OULREY: Okay, this level is 8-fold greater than the level in the 1986 draft EPA health assessment, due to DHS incorporation of recent analyses of human metabolism.

CHAIRMAN PITTS: We'd taken out metabolism,

hadn't we?

BOARD MEMBER GLANTZ: Well, it is okay.

BOARD MEMBER FROINES: I think, actually, at least an analyses of the uncertainty in human metabolism is actually what is correct, and I think it should stay that way.

BOARD MEMBER FRIEDMAN: Correct.

BOARD MEMBER GLANTZ: okay.

BOARD MEMBER FROINES: It is a --

BOARD MEMBER GLANTZ: All you do is just say that --

BOARD MEMBER FROINES: -- quantitative evaluation --

BOARD MEMBER GLANTZ: -- you just say --

BOARD MEMBER FROINES: -- it is a quantitative evaluation of uncertainty.

DR. GEORGE ALEXEEFF: The other thing is you could just be more specific and state that DHS incorporated a 25 percent upper bound on metabolism, as opposed to saying unclear with recent data, kind of concept.

CHAIRMAN PITTS: Why not, because if that is what you did was put 25 percent as exposure, versus that, and that makes a lot of sense to me, and then you can argue about what that is.

DR. GEORGE ALEXEEFF: Right, and then it is clear in case the data is shown the upper bounds is 20 next week, then we can adjust it.

[General discussion.]

BRUCE OULREY: Okay, so we will incorporate that, then.

CHAIRMAN PITTS: Well, you'd better read it.

BRUCE OULREY: George, would you repeat that?

[Pause in the proceedings.]

DR. GEORGE ALEXEEFF: Incorporation of a 25 percent upper bound on human metabolism.

CHAIRMAN PITTS: As against whatever the other number was.

BRUCE OULREY: A 25 percent upper bound on human metabolism?

CHAIRMAN PITTS: Right.

BOARD MEMBER BYUS: Right.

CHAIRMAN PITTS: Let's get it exactly what George says here now.

George.

DR. GEORGE ALEXEEFF: Incorporation of a 25 percent upper bound on human metabolism --

BOARD MEMBER GLANTZ: What is a 25 percent of metabolism?

DR. GEORGE ALEXEEFF: That is why I said, on.

Upper bound on metabolism. The metabolism rate is 25 percent, so we could say an upper bound on human metabolism at a rate of 25 percent.

BOARD MEMBER GLANTZ: Of perchloroethylene.

BOARD MEMBER FROINES: I frankly still feel that the sentence is unnecessary. I think you are really plaguing an issue that is going to drive us crazy before the Board, and I -- well, I asked that before, and people said, well, you have to say it because it was raised in the comments about that this is different than EPA.

I don't know if that -- if what we are doing is helping that. I really don't think it is. I think --

BOARD MEMBER BYUS: I think it would be helpful to the Board if you could specify why the DHS value is 8-fold greater than the EPA. That would be helpful.

BOARD MEMBER GLANTZ: Yeah, maybe that doesn't belong in the finding. In the findings -- every meeting the findings get longer. I mean, you could put that in the executive summary.

BOARD MEMBER FROINES: I think George should present that to the Board when he makes his presentation.

BOARD MEMBER BYUS: I don't have any problem with that,

CHAIRMAN PITTS: You don't have any problem with that? Why don't we delete using -- delete the

sentence in there?

BOARD MEMBER FROINES: Yes.

CHAIRMAN PITTS: Okay, yeah, is there any objection to that?

[No response.]

Do I hear one?

[No response.]

All right, then we will delete it.

BOARD MEMBER FROINES: I mean, this is research that I do. I can speak to it. That is not the issue.

ME. OULREY: Okay.

CHAIRMAN PITTS: Okay, good.

Other questions or comments?

[No response.]

John, do you have anything else?

BOARD MEMBER FROINES: No.

CHAIRMAN PITTS: The others here?

BOARD MEMBER SEIBER: Yes, I have got a question on number 9. Are we over that far yet?

CHAIRMAN PITTS: Well, we are as far as you want to go.

BOARD MEMBER SEIBER: In the first paragraph, you talk about 600 potential excess cancers, and that is a total. In the next paragraph you talk about 17. Is that per year, or per million, or -- is that per 1

million? That is 17 potential --

DR. JOAN DENTON: It says on the next page, the approximately 5.5 million people exposed.

BOARD MEMBER SEIBER: Yes, so that seems almost inconsequential, compared to the 600 in the paragraph before.

DR. JOAN DENTON: The 600 are the near source, the receptors closest to the source.

BOARD MEMBER SEIBER: It just doesn't seem to be adding a whole lot to be talking about 17, when you've talked 600 before.

BOARD MEMBER FRIEDMAN: They are just the 5.5 million who live near the source, whereas the --

CHAIRMAN PITTS: You see that --

BOARD MEMBER FRIEDMAN: -- others are spread all over the state.

CHAIRMAN PITTS: -- right, and that is next to hot spots.

BOARD MEMBER SEIBER: Well, if there are 30 million people in the state, and if there is only 17 among the hot spot people, how can there be 600 among the entire population? I just miss something here.

DR. JOAN DENTON: Right, and it is my mistake.

The 600 is for statewide, and the 17 of the potential cancer cases above background, due to near

source exposure.

BOARD MEMBER SEIBER: Well, even if I multiplied 17 by 6, I still don't get anywhere close to 600, so I am just having a hard time with the numbers.

BOARD MEMBER GLANTZ: Well, that is in addition to the 600, the proportion of the 600.

DR. JOAN DENTON: That is above background.

BOARD MEMBER SEIBER: Oh, I see --

DR. JOAN DENTON: You see, above, right --

BOARD MEMBER SEIBER: -- right.

DR. JOAN DENTON: -- above state wide.

BOARD MEMBER SEIBER: Oh, okay, 17 more than the 600 --

BOARD MEMBER GLANTZ: So, they are saying there are a proposed 617 altogether.

BOARD MEMBER SEIBER: Okay, well, that would make a little more logic to put something like that in.

DONALD AMES: Well, one of the primary points of the hot spot risk that we made during the presentation was that ambient levels for small groups of individuals nearer the hot spot facilities experience hot spot exposure on the order of, I think it was, 8 to 15 times higher than the general ambient exposure.

And, maybe that is a point we could make in here, rather than the 17. I know the 17 is very

confusing.

DR. JOAN DENTON: Because we are not saying --

DONALD AMES: See, because what portion of the 17 is from a few hundred, versus the 5 million --

DR. JOAN DENTON: Right.

DONALD AMES:-- and so forth, and one of the reasons we changed the presentation earlier was so that the panel would have an idea of how much higher those ambient levels are nearer the hot spot exposures, and I think the answer was somewhere in the range of 8 to 15 times higher for several hundred people, or in one case, a couple or 3000 people.

We could modify that per the discussion earlier.

BOARD MEMBER DAVIS: Could you put it in the clause above the 600 described above? It says above background. We are all having trouble with background.

Background is with no compound out there, normal folks. You mean background with the 600. In a strict sense you are saying above these 600 --

DONALD AMES: Above and beyond the 600 per excess cancers --

BOARD MEMBER GLANTZ: Due to the average ambient exposure.

DONALD AMES:-- we have the -- right, the 17 is

above and beyond that.

But, what I am suggesting is possibly -- if this is confusing to the panel -- take out the 17 and just simply address as we did in our presentation earlier, the hot spot exposures relative to the general ambient, say that in a range of -- that hot spot -- put exposures and risks are about 8 to 15 times higher than the state-wide average.

BOARD MEMBER FRIEDMAN: Well, then it gets me back to Jim's question. You would expect then that if 30 million people get 600 cases, roughly 5 million would get 100 cases. And, then why with this huge exposure, you only get 17 more?

DONALD AMES: Because the 17 is integrating the increased exposure out to the isoplat [sic.] so far that you include 5 million people.

The number I quoted, the 8 to 15 times higher are only experienced by a few hundred people. In one case it was 600, I think, and in the other case, in the other city we modeled, it was about 2500 people experiencing that elevated risk, and not the 5 million.

So, it just depends on how far you carry out that integration.

BOARD MEMBER FROINES: Can I ask you a question about that --

DONALD AMES: Yes.

BOARD MEMBER FROINES: -- and this is becoming more confusing.

You have modeled Burbank and -- what's the other place?

BARBARA COOK: City of Industry.

BOARD MEMBER FROINES: City of Industry. Those are the two places you've modeled. Now, if you actually modeled places in northern California and in San Diego, and wherever, might you not find other hot spots with the same kind of thing?

DONALD AMES: Certainly.

BOARD MEMBER FROINES: Well, then it seems to me -- then I really get confused about this 17 figure, because it could be much larger --

DONALD AMES: Oh, certainly, we would expect it would be much larger, not until we have the outcome of the --

BOARD MEMBER FROINES: Because I don't think this meets the issue at all.

DONALD AMES: Yes, right, I would agree with that. Just based on available information in the modeling we were able to do for the identification process, you know, in some cases like in benzene previously, we estimated hot spot exposure were double

ambient. In this case, it is 8 to 15 times ambient for the sources modeled. And, certainly, they could be higher. And, certainly they could be higher, for example in --

BOARD MEMBER GLANTZ: You know, I think, based on this discussion, I think that paragraph should be deleted because it is confusing.

And, if you go up to number 8, to say ARB -- if you will look at number 8, ARB staff estimated exposure of near source modeling 8, blah, blah, blah. You know, results showed individuals could be exposed to levels significantly above background, in the range of -- whatever -- with the attendant increase in risk, or something. Without putting in the numbers, and then delete that paragraph that begins at the bottom of page 4, just delete it.

CHAIRMAN PITTS: Do you have any problems with that?

BOARD MEMBER GLANTZ: Because that makes the point that there could be significant hot spots, but without putting any numbers in there.

CHAIRMAN PITTS: Okay, fine, I think that is the general --

BOARD MEMBER FROINES: But, I think it would be worth saying also, to add another sentence that says --

we all should keep in mind that this is our document, so we should decide what we want in it, because it is what we are going to say to them, and I think the panel should say that we think additional modeling of hot spot exposures would be appropriate, given what has already been found.

CHAIRMAN PITTS: Exactly, and that is what we did with dioxin, exactly what we did, additional modeling, and experimental data to make sure that --

[General discussion.]

-- it is not hard to get.

BOARD MEMBER SEIBER: Including a production facility, which are almost totally -- well, they are totally ignored in this document.

DONALD AMES: Would the panel like to say something like, this suggests, after saying individuals could be exposed to levels significantly above background. Something like, this suggests that additional modeling is warranted for risk management purposes.

CHAIRMAN PITTS: Well, I think the accumulation of experimental data, I mean, you could make the measurements in a straightforward manner. So, I think additional -- acquisition of additional data levels, and associate -- as for input to models, or input to model

would seem appropriate, is appropriate.

DR. JOAN DENTON: So, to clarify, it would be the end of the Finding Number 8, and we could say, acquisition of additional data as input to models is appropriate?

BOARD MEMBER GLANTZ: Well, I think John wanted to say something stronger than that. I think you wanted to say that, something like, in light of the presence of these hot spots, okay, there should be, you know, the ARB should extend its modeling and data collection activities, you know, more broadly throughout the state.

BOARD MEMBER BYES: Would you repeat that again. Extend its --

BOARD MEMBER GLANTZ: Its modeling and data collection throughout the state, or more broadly in the state, or something like that.

BOARD MEMBER FROINES: You don't have to do that, though.

[Voice fades out of hearing range.]

[General discussion.]

CHAIRMAN PITTS: Okay?

DONALD AMES: Okay.

CHAIRMAN PITTS: Fine.

Are there other changes?

[No response.]

If not, then I shall --

BOARD MEMBER SEIBER: Just a minute, yes, I have one other comment.

In number 11, I am not very well swayed by the difference between the indoor and the outdoor concentrations. You make a big point of it, but the numbers don't seem different enough to say whether they are statistically different or not. You are talking about an indoor range of .34 to 1.01 versus the outdoor range of .26 to .66. Are those really statistically different? Can we make a strong statement with that? For one thing, they are small differences; secondly, are they statistically different?

DR. JOAN DENTON: We have other studies, that have shown even greater differences than that, so we are confident saying that perchloroethylene exposures can be higher indoors than outdoors, and relying on this matched data, where they did indoor and outdoor simultaneously, these were the differences that were observed.

BOARD MEMBER SEIBER: As an analytical chemist, I am just not very swayed by those numerical difference as showing any great difference in the indoor and outdoor. You may have other data that is better.

CHAIRMAN PITTS: Would you just want to leave it in and say that other levels of exposure can vary

among, and leave out those, the data, I mean.

BOARD MEMBER SEIBER: Maybe just leave the numbers out --

CHAIRMAN PITTS: Sure, leave the numbers out.

BOARD MEMBER SEIBER: -- because there is the statement that there is evidence.

CHAIRMAN PITTS: It is higher indoors, and just let it go at that.

Are you agreeing with that?

[No response.]

So, we will just take out, starting with "in a". That is a good point, and I looked at those too, and I was wondering what they would do.

Are there other questions?

[No response.]

If not, I would like -- let's be sure everyone has been heard from here?

All right, if not, it has been moved and seconded, that would be, modifications as indicated that we accept the findings.

All those in favor, please raise your hand?

[All hands raised.]

Those opposed?

[No hands raised.]

It carries unanimously.

Now, we have a question as to -- Bill Lockett, do we have -- on the future meeting dates, is that essential at this time?

If not, I would like to see that our colleagues to the north get that cap, but Lane will probably shoot me if I do.

WILLIAM LOCKETT: The next meeting is July 25 for formaldehyde. Yes, with a 12:00 noon start, in northern California, with no planned August meeting. Most people are gone in August, I can see from taking a poll.

You do have calendars in your folders, and to the extent you can fill them out for the rest of the year, that would be very helpful.

We need a date in September for 1,3-butadiene, and that is why it would be helpful if you would turn your calendars in so we can set that as soon as we can.

And, I didn't look at the findings again. What I understand is that by adopting the findings, that means that the reports are acceptable to the panel.

BOARD MEMBER GLANTZ: I move that the reports are not seriously deficient, subject to the changes that have been made.

CHAIRMAN PITTS: Subject to the changes that were made during the discussion.

COUNSEL WALSH: The findings actually include that summation.

BOARD MEMBER GLANTZ: Yeah, that is true.

CHAIRMAN PITTS: Okay, fine --

BOARD MEMBER GLANTZ: Forget it.

CHAIRMAN PITTS: -- that is why it is there.

For those of you who have to catch a plane, thank you very much, and for those who want lunch it is in there.

WILLIAM LOCKETT: Yes.

BOARD MEMBER FROINES: But, we may not have a July meeting, right?

CHAIRMAN PITTS: Right.

DR. JOAN DENTON: That is correct.

[General Discussion.]

BRUCE OULREY: But, at this point in time we are planning on it, and if it changes we will let you know.

[Whereupon the meeting was concluded at 1:10 p.m.]

R E P O R T E R 'S C E R T I F I C A T E

STATE OF CALIFORNIA)
) ss.
COUNTY OF MADERA)

I, PRISCILLA PIKE, Hearing Reporter for the State of California, do hereby certify that the foregoing pages comprise a full, true and correct transcript of the proceedings as reflected therein.

Dated: June 17, 1991

Priscilla Pike

PRISCILLA PIKE
Hearing Reporter
Notary Public